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Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: MARK BERCH Examiner # : 59193 Date: 6/13/07

Art Unit: 1624 Phone Number: 2-0663 Serial Number: 10533183

Location (Bldg/Room#): 5C01 (Mailbox #): 5C18 Results Format Preferred (circle): PAPER DISK

****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: _____

Inventors (please provide full names): _____

_____

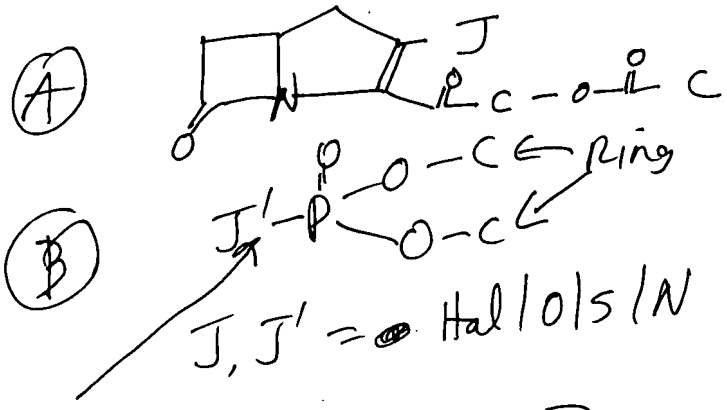
Earliest Priority Date: _____

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only ***Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.***

CAS React



done in Care
Fm 1 cmpd is not indexed as such in ref

Search A + B

****

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: _____	____ NA Sequence (#)	____ STN ____ Dialog
Searcher Phone #: _____	____ AA Sequence (#)	____ Questel/Orbit ____ Lexis/Nexis
Searcher Location: _____	____ Structure (#)	____ Westlaw ____ WWW/Internet
Date Searcher Picked Up: _____	____ Bibliographic	____ In-house sequence systems
Date Completed: _____	____ Litigation	____ Commercial ____ Oligomer ____ Score/Length ____ Interference ____ SPDI ____ Encode/Transl
Searcher Prep & Review Time: _____	____ Fulltext	____ Other (specify)
Online Time: _____	____ Other	

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=> fil casreact
FILE 'CASREACT' ENTERED AT 09:25:59 ON 15 JUN 2007
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FILE CONTENT:1840 - 9 Jun 2007 VOL 146 ISS 25

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*************************************************************
*                                                           *
*     CASREACT now has more than 12 million reactions       *
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Some CASREACT records are derived from the ZIC/VINITI database (1974-1999)
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This file contains CAS Registry Numbers for easy and accurate substance
identification.

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L1                STR
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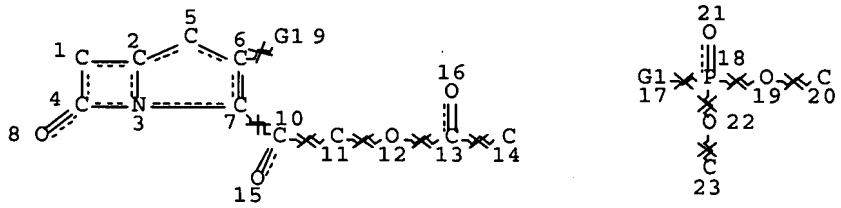


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NSPEC    IS R      AT  23
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  23

STEREO ATTRIBUTES: NONE
L3             0 SEA FILE=CASREACT SSS FUL L1 (     0 REACTIONS)


=> d que l8
L6                STR
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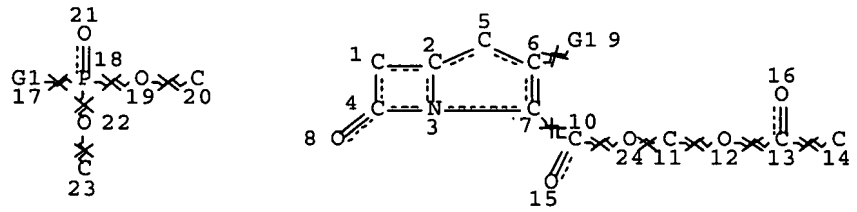

VAR G1=X/O/S/N
NODE ATTRIBUTES:
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NSPEC IS R AT 23
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

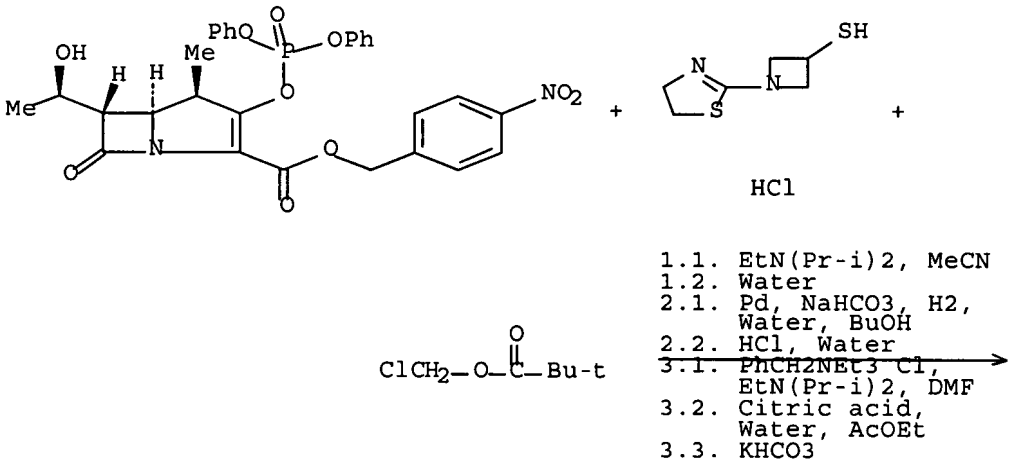
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE
L8 4 SEA FILE=CASREACT SSS FUL L6 (90 REACTIONS)

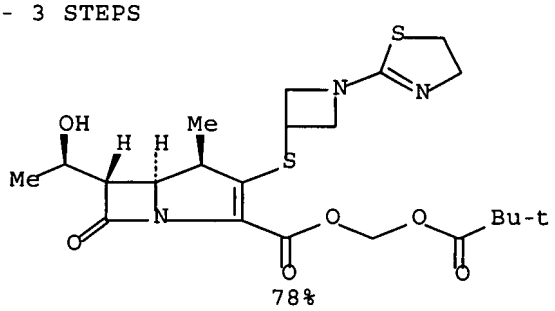
=> d l8 ibib abs crd tot

L8 ANSWER 1 OF 4 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:335815 CASREACT Full-text
TITLE: Syntheses and pharmacokinetic studies of prodrug esters for the development of oral carbapenem, L-084
AUTHOR(S): Isoda, Takeshi; Ushirogochi, Hideki; Satoh, Koichi; Takasaki, Tsuyoshi; Yamamura, Itsuki; Sato, Chisato; Mihira, Ado; Abe, Takao; Tamai, Satoshi; Yamamoto, Shigeki; Kumagai, Toshio; Nagao, Yoshimitsu
CORPORATE SOURCE: Medical Research Laboratories, Wyeth K.K., 1-6-34 Kashiwa-cho, Shiki-shi, Saitama, 353-8511, Japan
SOURCE: Journal of Antibiotics (2006), 59(4), 241-247
CODEN: JANTAJ; ISSN: 0021-8820
PUBLISHER: Japan Antibiotics Research Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We discovered an orally active carbapenem, L-084, through pharmacokinetic studies on various prodrug esters of (1R,5S,6S)-6-[(R)-1-hydroxyethyl]-1-methyl-2-[1-(1,3-thiazolin-2-yl)azetidin-3-yl]thio-1-carbapen-2-em-3-carboxylic acid (LJC11,036). L-084 showed a strong antimicrobial activity against Gram-pos. and Gram-neg. bacteria and exhibited the highest intestinal absorption among synthesized prodrugs of LJC11,036.

RX(38) OF 126 - 3 STEPS

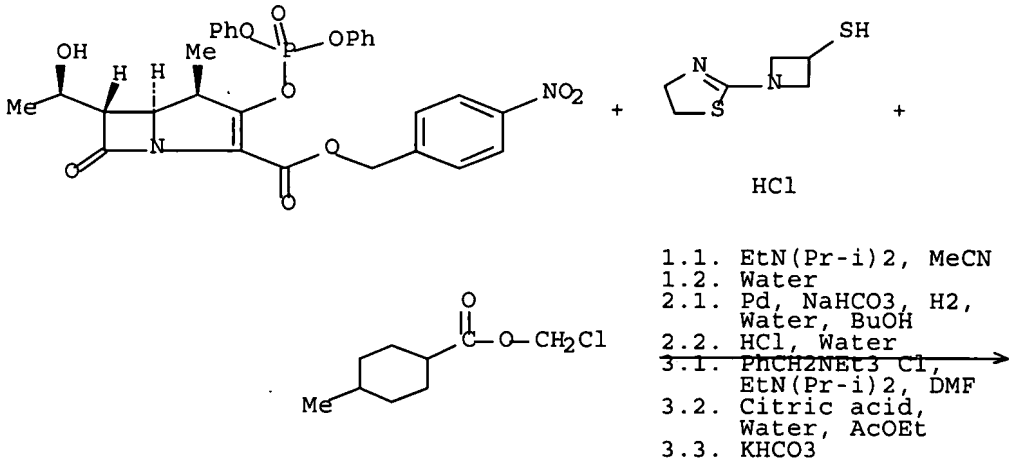


RX(38) OF 126 - 3 STEPS

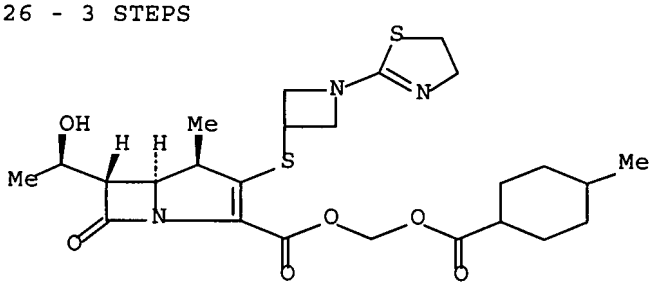


CON: STEP(1.1) 2 hours, -20 deg C
STEP(1.2) 0.5 hours, 5 deg C
STEP(2.1) 1.5 hours, room temperature, 400 kPa
STEP(2.2) pH 5.6
STEP(3.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(3.2) 5 deg C, pH 4
STEP(3.3) pH 7.6

RX(39) OF 126 - 3 STEPS



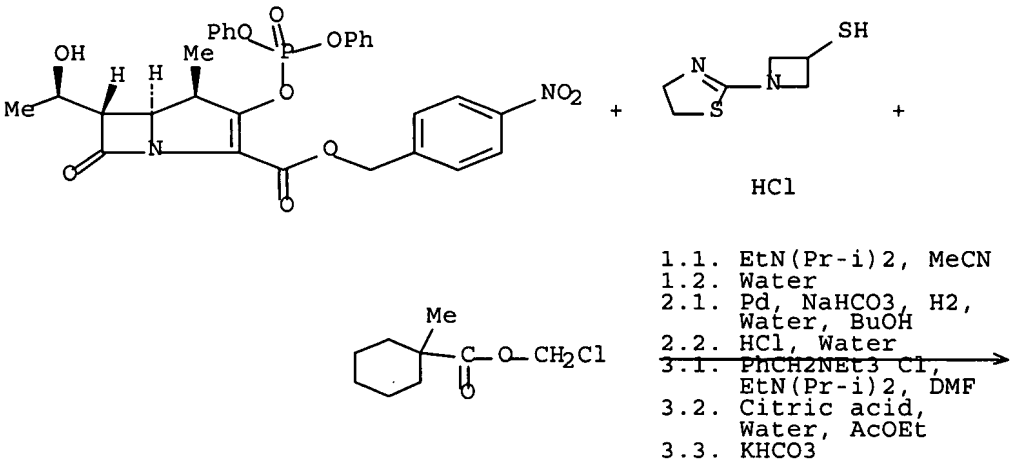
RX(39) OF 126 - 3 STEPS



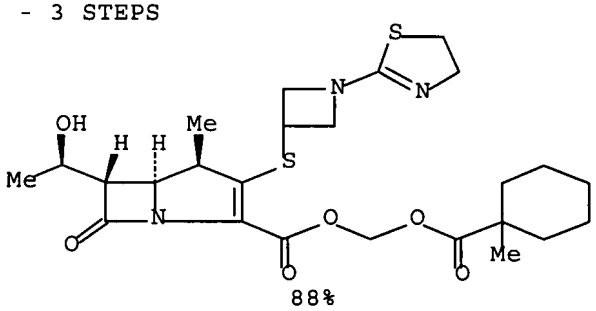
80%

CON: STEP(1.1) 2 hours, -20 deg C
STEP(1.2) 0.5 hours, 5 deg C
STEP(2.1) 1.5 hours, room temperature, 400 kPa
STEP(2.2) pH 5.6
STEP(3.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(3.2) 5 deg C, pH 4
STEP(3.3) pH 7.6

RX(41) OF 126 - 3 STEPS



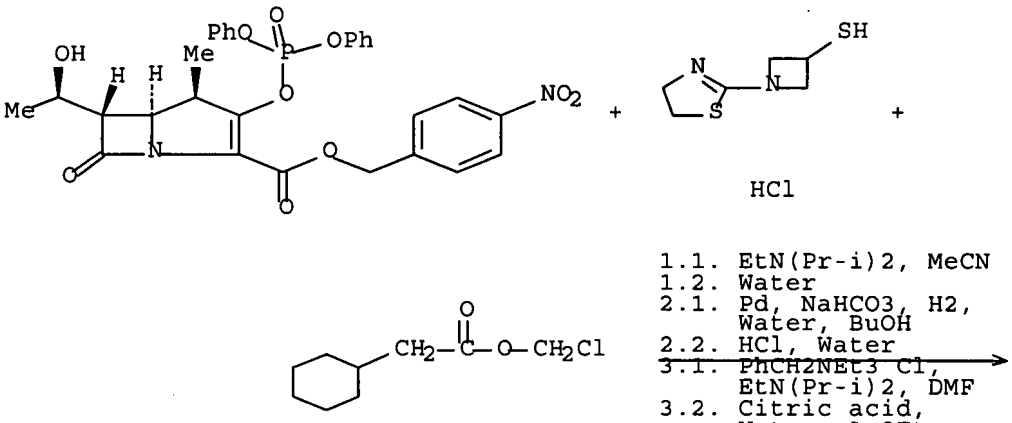
RX(41) OF 126 - 3 STEPS



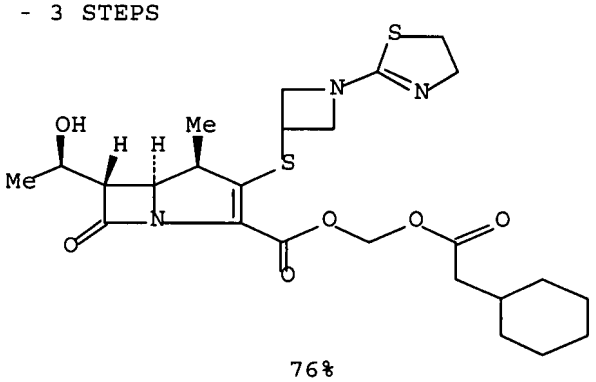
88%

CON: STEP(1.1) 2 hours, -20 deg C
STEP(1.2) 0.5 hours, 5 deg C
STEP(2.1) 1.5 hours, room temperature, 400 kPa
STEP(2.2) pH 5.6
STEP(3.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(3.2) 5 deg C, pH 4
STEP(3.3) pH 7.6

RX(42) OF 126 - 3 STEPS



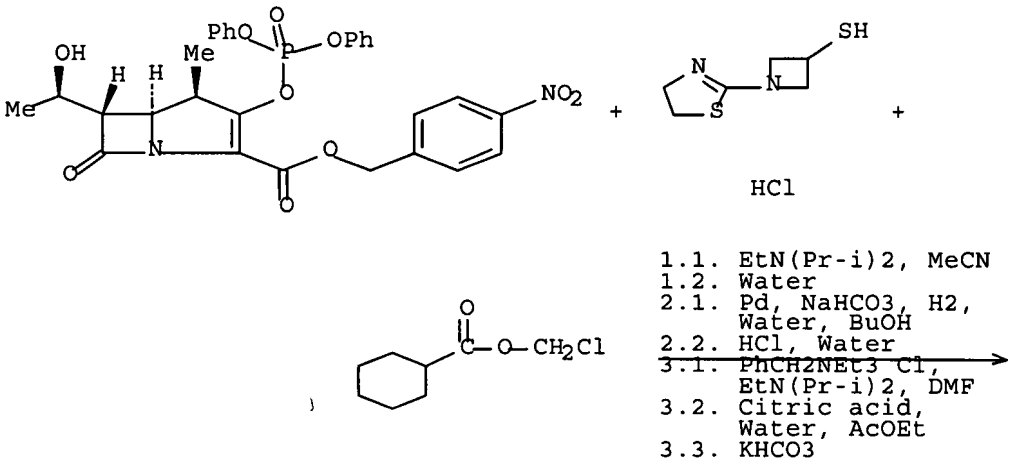
RX(42) OF 126 - 3 STEPS



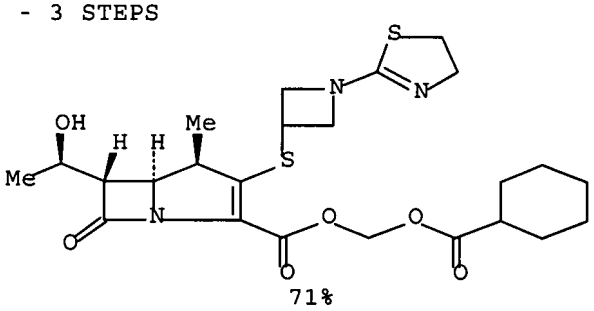
76%

CON: STEP(1.1) 2 hours, -20 deg C
STEP(1.2) 0.5 hours, 5 deg C
STEP(2.1) 1.5 hours, room temperature, 400 kPa
STEP(2.2) pH 5.6
STEP(3.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(3.2) 5 deg C, pH 4
STEP(3.3) pH 7.6

RX(43) OF 126 - 3 STEPS



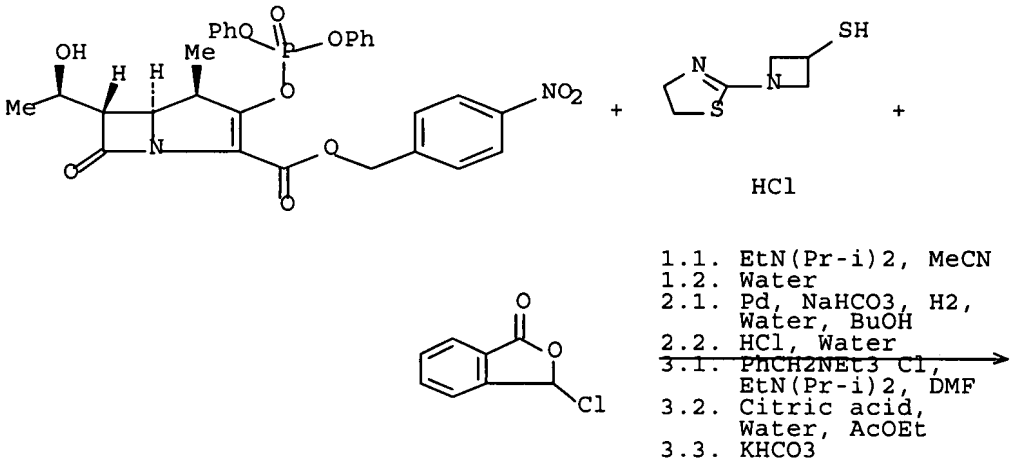
RX(43) OF 126 - 3 STEPS



71%

CON: STEP(1.1) 2 hours, -20 deg C
STEP(1.2) 0.5 hours, 5 deg C
STEP(2.1) 1.5 hours, room temperature, 400 kPa
STEP(2.2) pH 5.6
STEP(3.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(3.2) 5 deg C, pH 4
STEP(3.3) pH 7.6

RX(45) OF 126 - 3 STEPS



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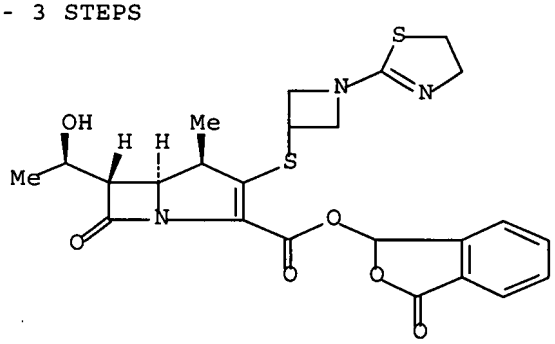
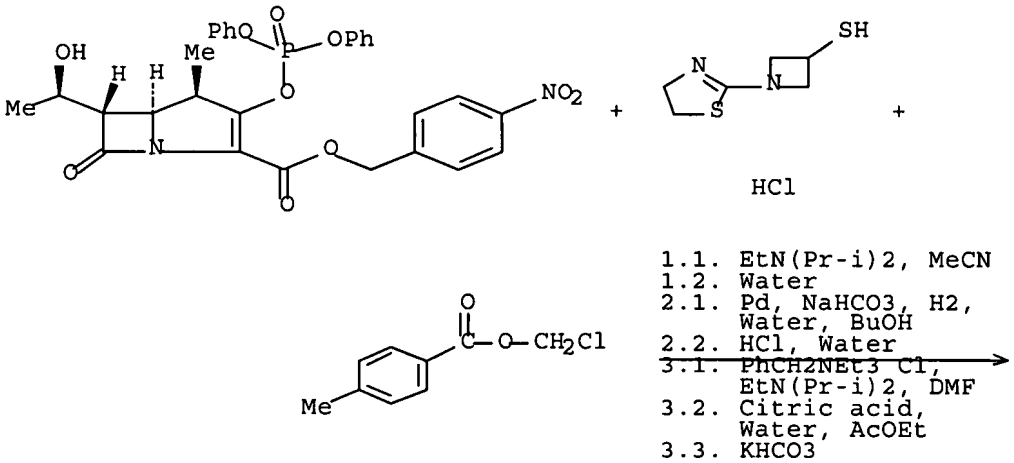


84%

CON: STEP(1.1) 2 hours, -20 deg C
STEP(1.2) 0.5 hours, 5 deg C
STEP(2.1) 1.5 hours, room temperature, 400 kPa
STEP(2.2) pH 5.6
STEP(3.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(3.2) 5 deg C, pH 4
STEP(3.3) pH 7.6

RX(46) OF 126 - 3 STEPS



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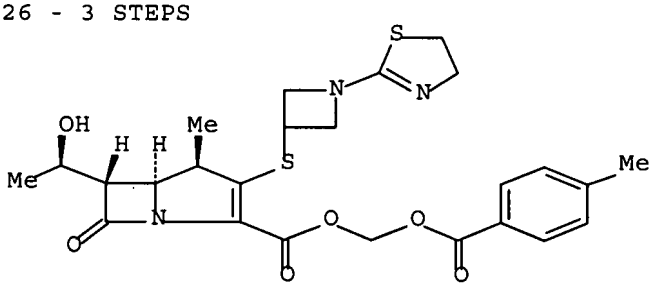
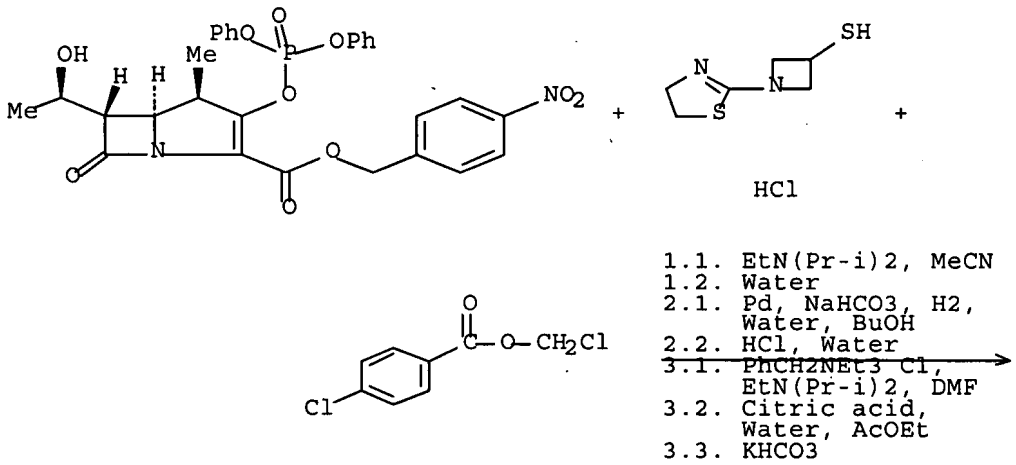


84%

CON: STEP(1.1) 2 hours, -20 deg C
STEP(1.2) 0.5 hours, 5 deg C
STEP(2.1) 1.5 hours, room temperature, 400 kPa
STEP(2.2) pH 5.6
STEP(3.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(3.2) 5 deg C, pH 4
STEP(3.3) pH 7.6

RX(47) OF 126 - 3 STEPS



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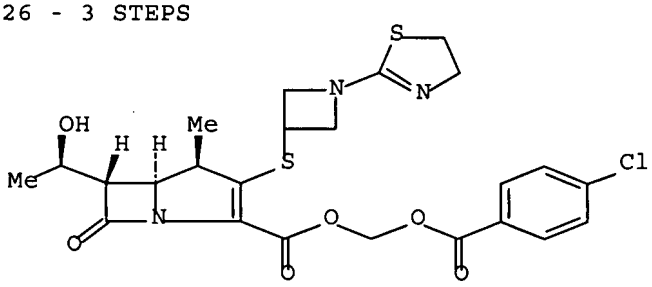
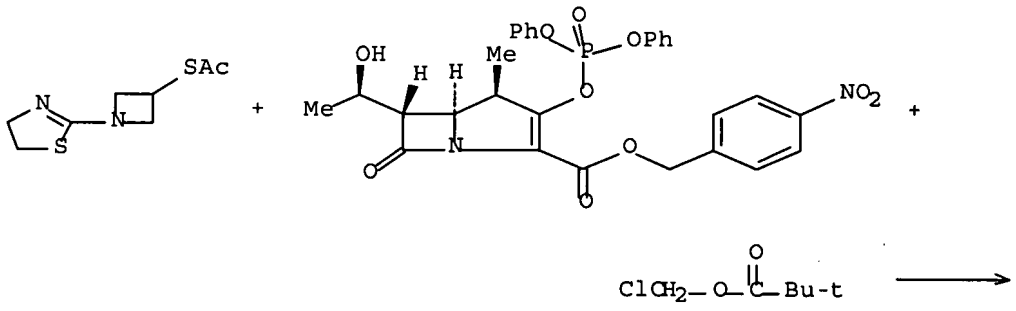


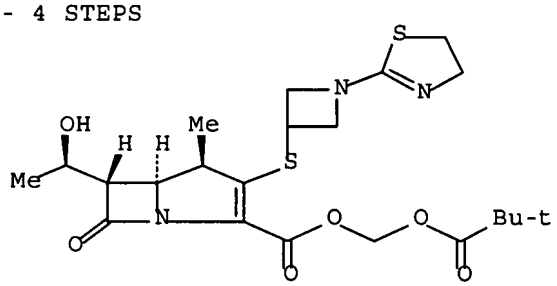
81%

CON: STEP(1.1) 2 hours, -20 deg C
STEP(1.2) 0.5 hours, 5 deg C
STEP(2.1) 1.5 hours, room temperature, 400 kPa
STEP(2.2) pH 5.6
STEP(3.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(3.2) 5 deg C, pH 4
STEP(3.3) pH 7.6

RX(48) OF 126 - 4 STEPS



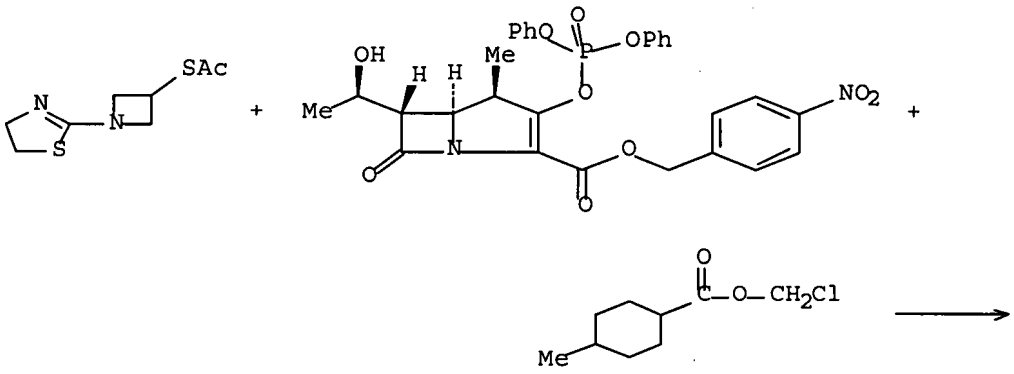
RX(48) OF 126 - 4 STEPS



78%

CON: STEP(1.1) 10 minutes, 5 deg C
STEP(1.2) 15 minutes
STEP(2.1) 2 hours, -20 deg C
STEP(2.2) 0.5 hours, 5 deg C
STEP(3.1) 1.5 hours, room temperature, 400 kPa
STEP(3.2) pH 5.6
STEP(4.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(4.2) 5 deg C, pH 4
STEP(4.3) pH 7.6

RX(49) OF 126 - 4 STEPS



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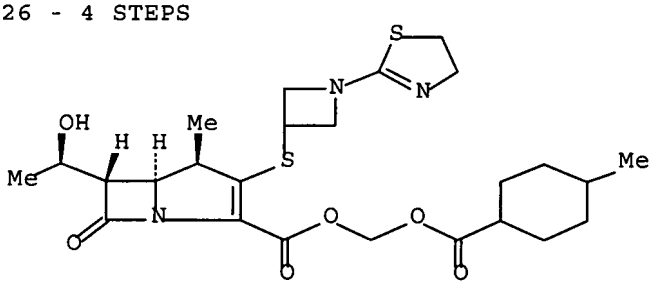

80%

CON: STEP(1.1) 10 minutes, 5 deg C
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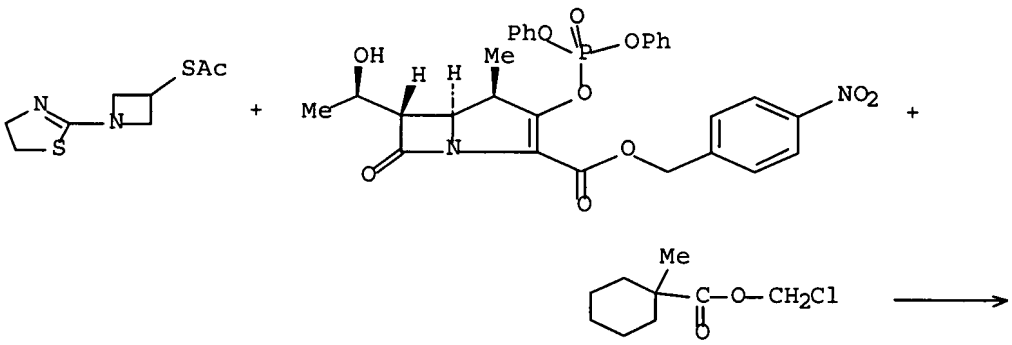
STEP(2.1) 2 hours, -20 deg C
STEP(2.2) 0.5 hours, 5 deg C
STEP(3.1) 1.5 hours, room temperature, 400 kPa
STEP(3.2) pH 5.6
STEP(4.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(4.2) 5 deg C, pH 4
STEP(4.3) pH 7.6

RX(51) OF 126 - 4 STEPS



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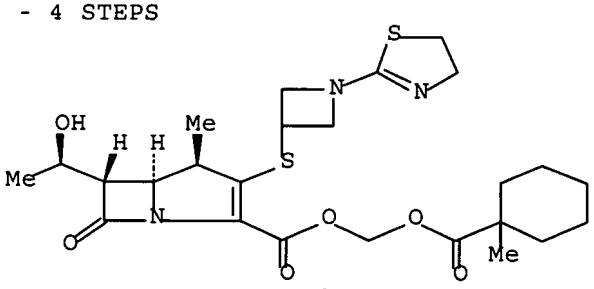
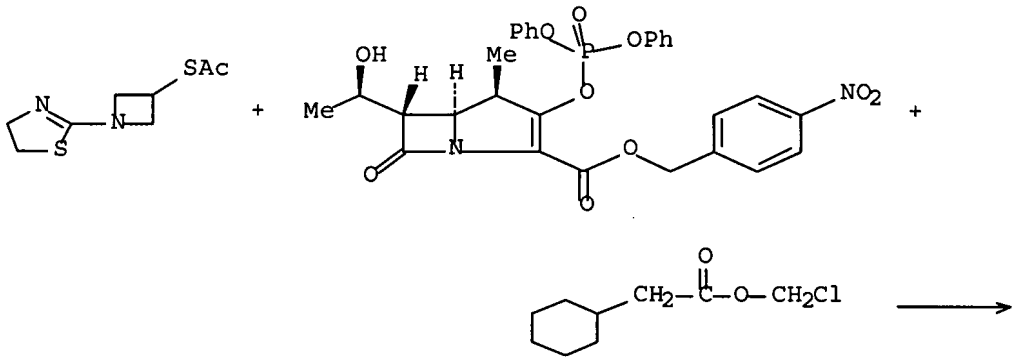


88%

CON: STEP(1.1) 10 minutes, 5 deg C
STEP(1.2) 15 minutes
STEP(2.1) 2 hours, -20 deg C
STEP(2.2) 0.5 hours, 5 deg C
STEP(3.1) 1.5 hours, room temperature, 400 kPa
STEP(3.2) pH 5.6
STEP(4.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(4.2) 5 deg C, pH 4
STEP(4.3) pH 7.6

RX(52) OF 126 - 4 STEPS



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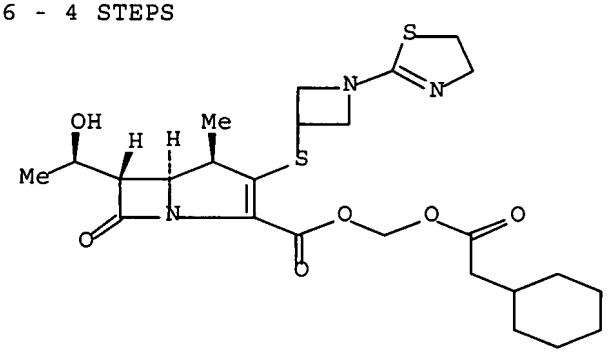

76%

CON: STEP(1.1) 10 minutes, 5 deg C
STEP(1.2) 15 minutes
STEP(2.1) 2 hours, -20 deg C
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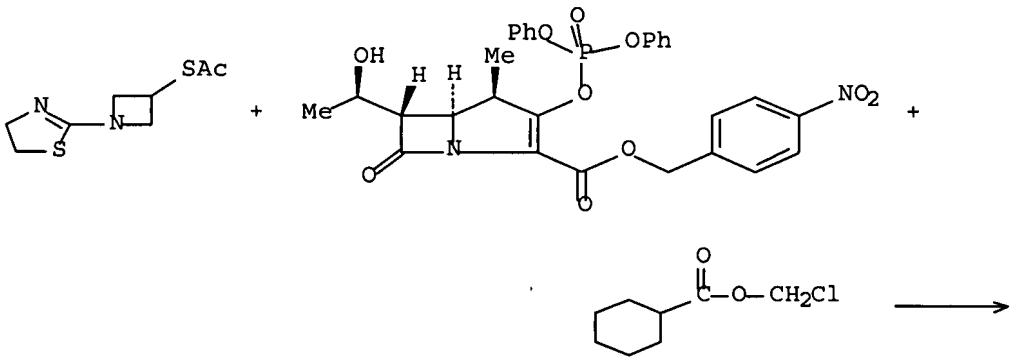
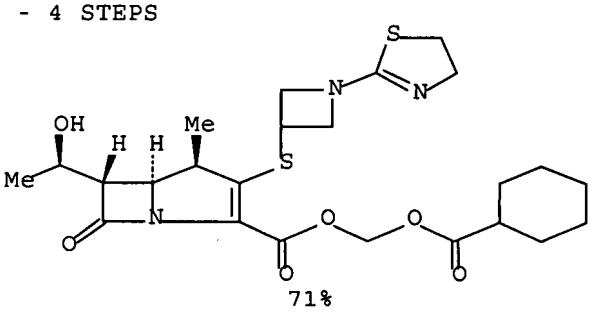
STEP(3.2) pH 5.6
STEP(4.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(4.2) 5 deg C, pH 4
STEP(4.3) pH 7.6

RX(53) OF 126 - 4 STEPS



RX(53) OF 126 - 4 STEPS



71%

CON: STEP(1.1) 10 minutes, 5 deg C
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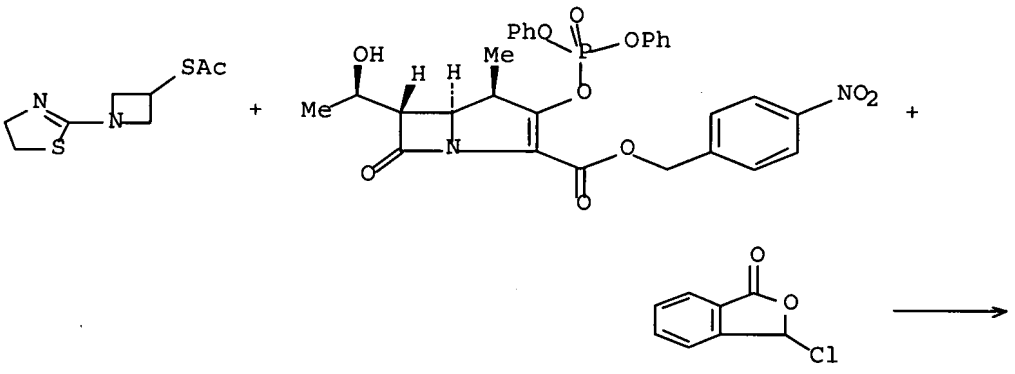
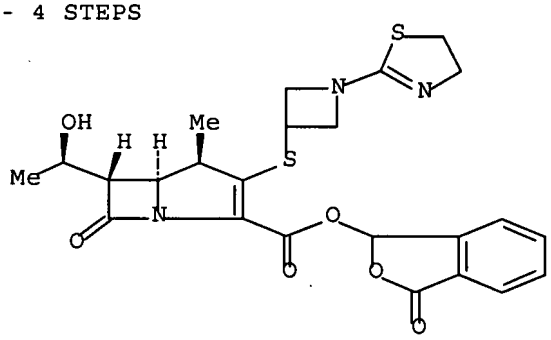
STEP(3.1) 1.5 hours, room temperature, 400 kPa
STEP(3.2) pH 5.6
STEP(4.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(4.2) 5 deg C, pH 4
STEP(4.3) pH 7.6

RX(55) OF 126 - 4 STEPS



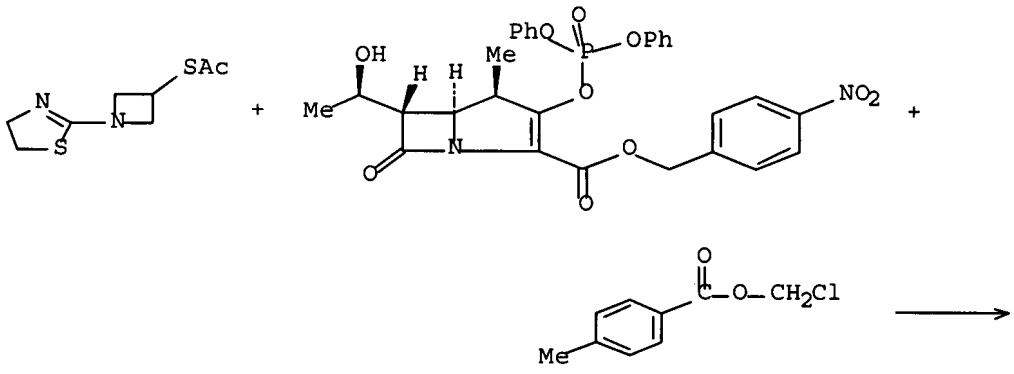
RX(55) OF 126 - 4 STEPS



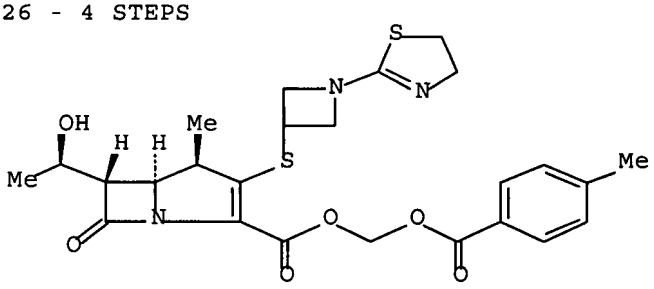
84%

CON: STEP(1.1) 10 minutes, 5 deg C
STEP(1.2) 15 minutes
STEP(2.1) 2 hours, -20 deg C
STEP(2.2) 0.5 hours, 5 deg C
STEP(3.1) 1.5 hours, room temperature, 400 kPa
STEP(3.2) pH 5.6
STEP(4.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(4.2) 5 deg C, pH 4
STEP(4.3) pH 7.6

RX(56) OF 126 - 4 STEPS



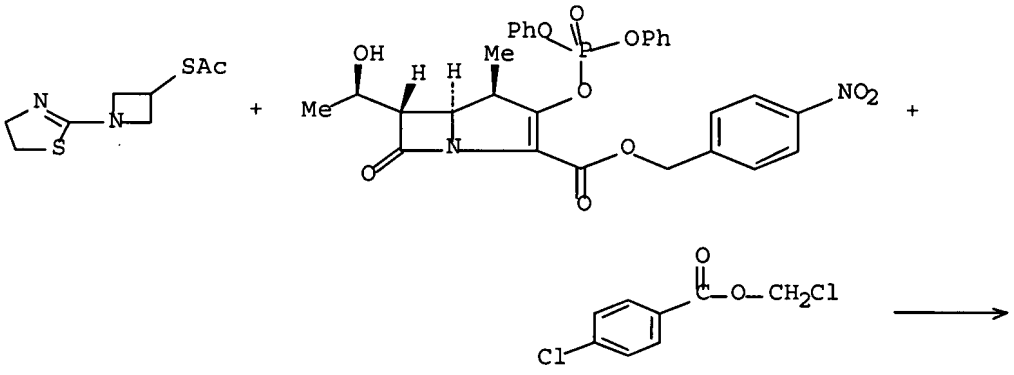
RX(56) OF 126 - 4 STEPS



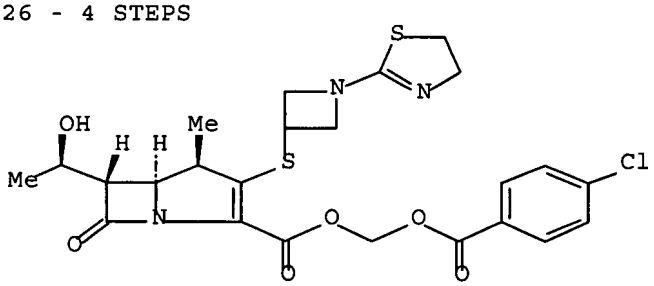
84%

CON: STEP(1.1) 10 minutes, 5 deg C
STEP(1.2) 15 minutes
STEP(2.1) 2 hours, -20 deg C
STEP(2.2) 0.5 hours, 5 deg C
STEP(3.1) 1.5 hours, room temperature, 400 kPa
STEP(3.2) pH 5.6
STEP(4.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(4.2) 5 deg C, pH 4
STEP(4.3) pH 7.6

RX(57) OF 126 - 4 STEPS



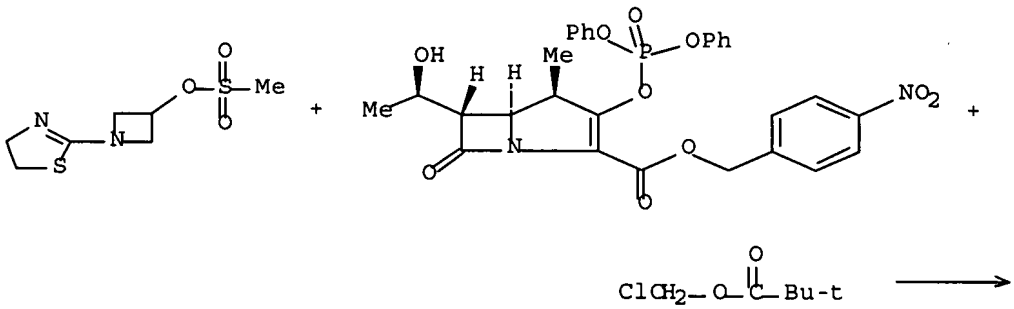
RX(57) OF 126 - 4 STEPS



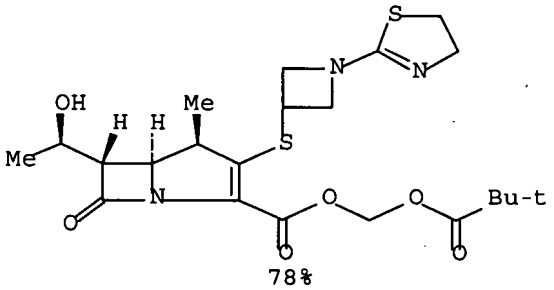
81%

CON: STEP(1.1) 10 minutes, 5 deg C
STEP(1.2) 15 minutes
STEP(2.1) 2 hours, -20 deg C
STEP(2.2) 0.5 hours, 5 deg C
STEP(3.1) 1.5 hours, room temperature, 400 kPa
STEP(3.2) pH 5.6
STEP(4.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(4.2) 5 deg C, pH 4
STEP(4.3) pH 7.6

RX(67) OF 126 - 5 STEPS



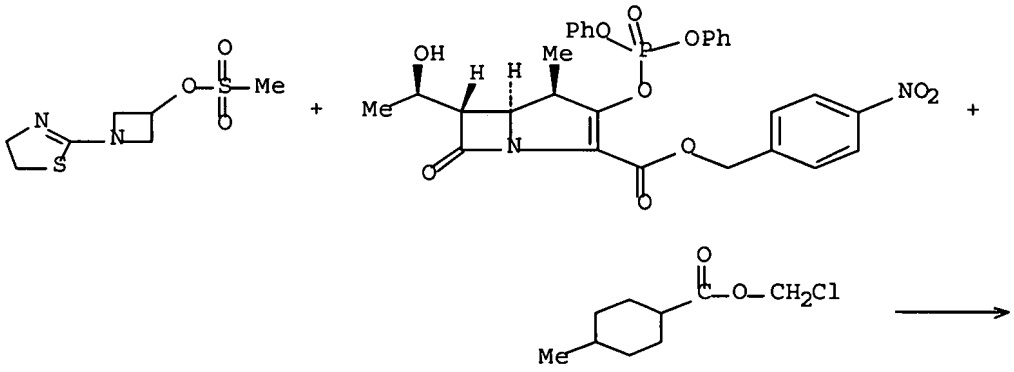
RX(67) OF 126 - 5 STEPS



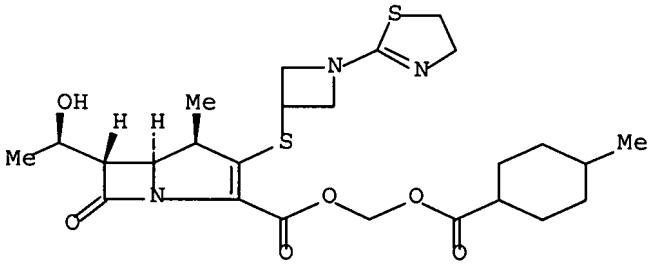
78%

CON: STEP(1) 5.5 hours, 100 deg C
STEP(2.1) 10 minutes, 5 deg C
STEP(2.2) 15 minutes
STEP(3.1) 2 hours, -20 deg C
STEP(3.2) 0.5 hours, 5 deg C
STEP(4.1) 1.5 hours, room temperature, 400 kPa
STEP(4.2) pH 5.6
STEP(5.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(5.2) 5 deg C, pH 4
STEP(5.3) pH 7.6

RX(68) OF 126 - 5 STEPS



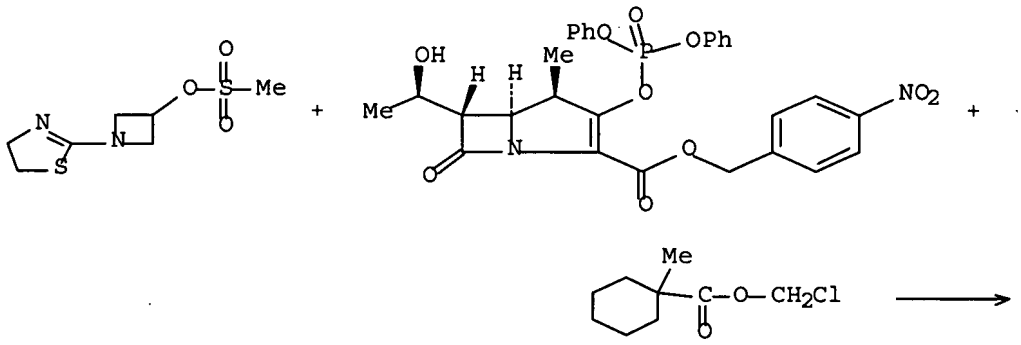
RX(68) OF 126 - 5 STEPS



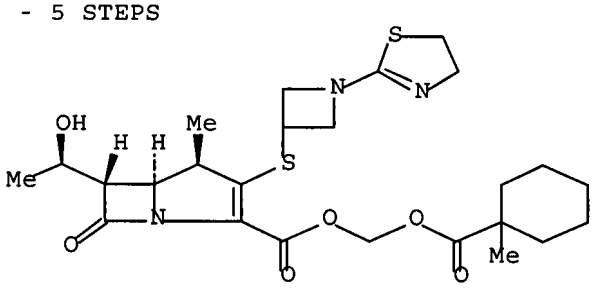
80%

CON: STEP(1) 5.5 hours, 100 deg C
STEP(2.1) 10 minutes, 5 deg C
STEP(2.2) 15 minutes
STEP(3.1) 2 hours, -20 deg C
STEP(3.2) 0.5 hours, 5 deg C
STEP(4.1) 1.5 hours, room temperature, 400 kPa
STEP(4.2) pH 5.6
STEP(5.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(5.2) 5 deg C, pH 4
STEP(5.3) pH 7.6

RX(70) OF 126 - 5 STEPS



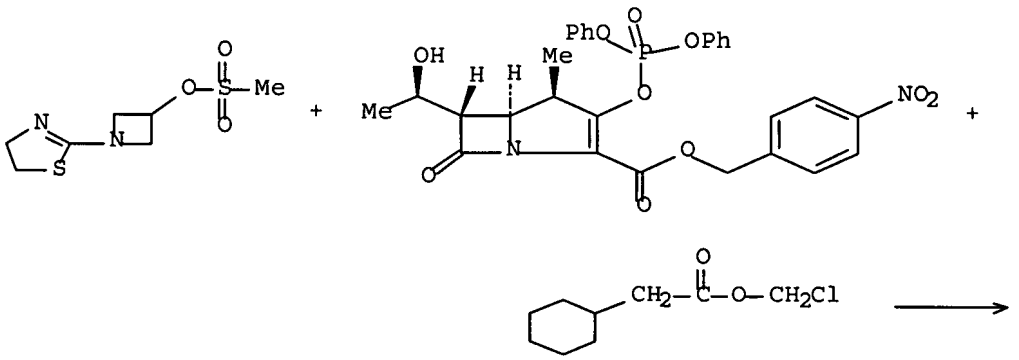
RX(70) OF 126 - 5 STEPS



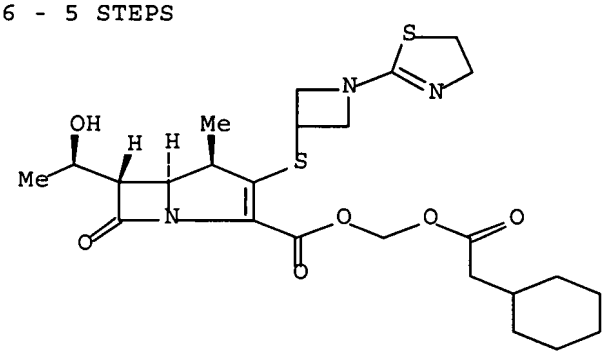
88%

CON: STEP(1) 5.5 hours, 100 deg C
STEP(2.1) 10 minutes, 5 deg C
STEP(2.2) 15 minutes
STEP(3.1) 2 hours, -20 deg C
STEP(3.2) 0.5 hours, 5 deg C
STEP(4.1) 1.5 hours, room temperature, 400 kPa
STEP(4.2) pH 5.6
STEP(5.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(5.2) 5 deg C, pH 4
STEP(5.3) pH 7.6

RX(71) OF 126 - 5 STEPS



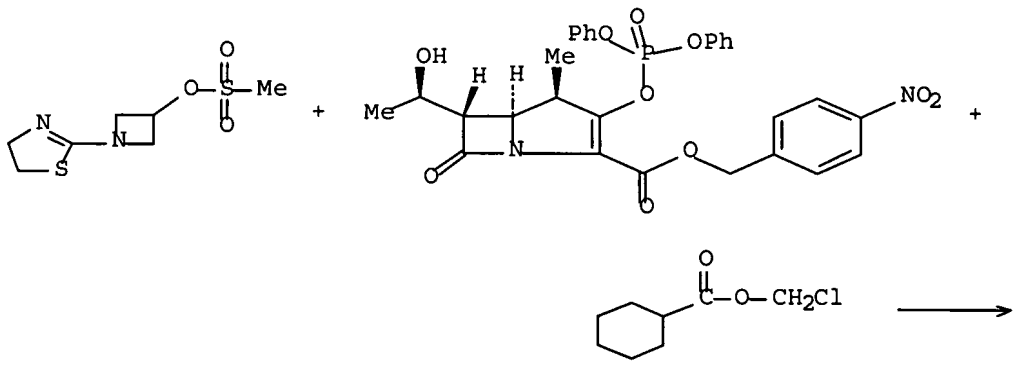
RX(71) OF 126 - 5 STEPS



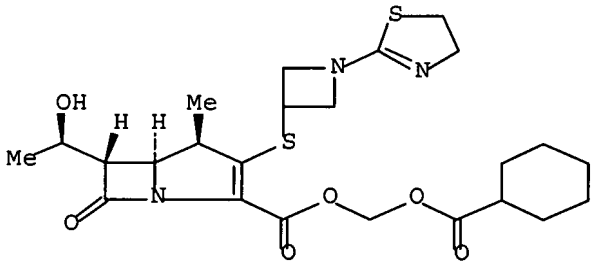
76%

CON: STEP(1) 5.5 hours, 100 deg C
STEP(2.1) 10 minutes, 5 deg C
STEP(2.2) 15 minutes
STEP(3.1) 2 hours, -20 deg C
STEP(3.2) 0.5 hours, 5 deg C
STEP(4.1) 1.5 hours, room temperature, 400 kPa
STEP(4.2) pH 5.6
STEP(5.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(5.2) 5 deg C, pH 4
STEP(5.3) pH 7.6

RX(72) OF 126 - 5 STEPS



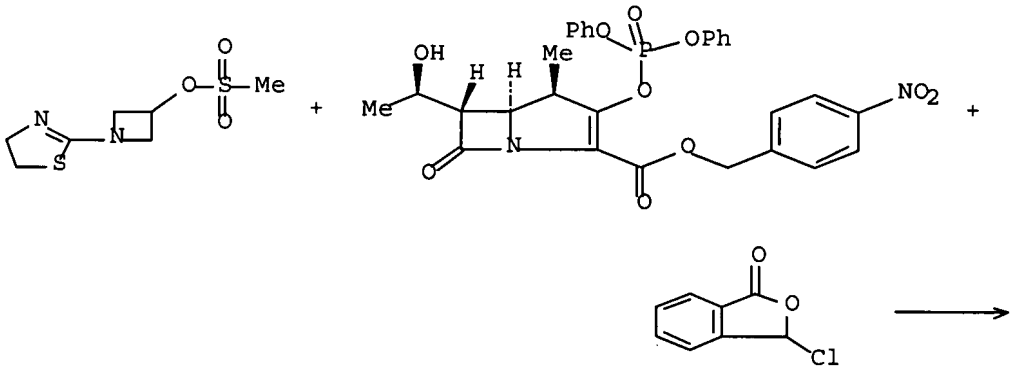
RX(72) OF 126 - 5 STEPS



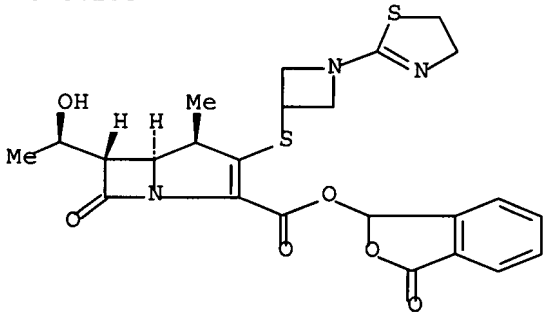
71%

CON: STEP(1) 5.5 hours, 100 deg C
STEP(2.1) 10 minutes, 5 deg C
STEP(2.2) 15 minutes
STEP(3.1) 2 hours, -20 deg C
STEP(3.2) 0.5 hours, 5 deg C
STEP(4.1) 1.5 hours, room temperature, 400 kPa
STEP(4.2) pH 5.6
STEP(5.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(5.2) 5 deg C, pH 4
STEP(5.3) pH 7.6

RX(74) OF 126 - 5 STEPS



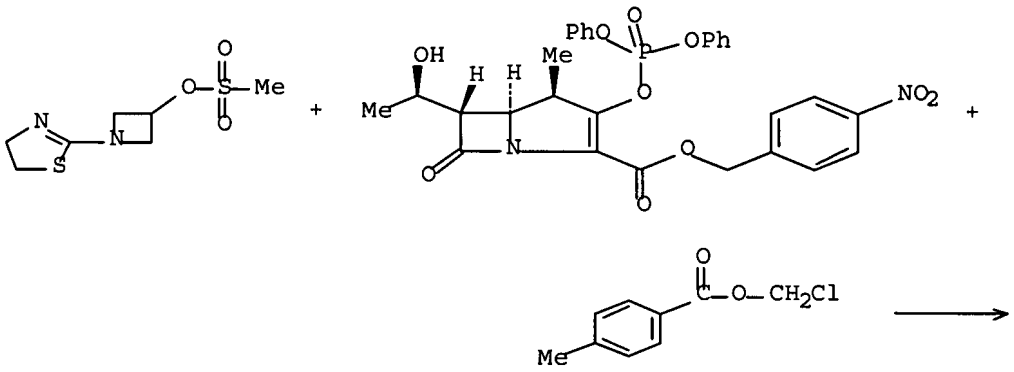
RX(74) OF 126 - 5 STEPS



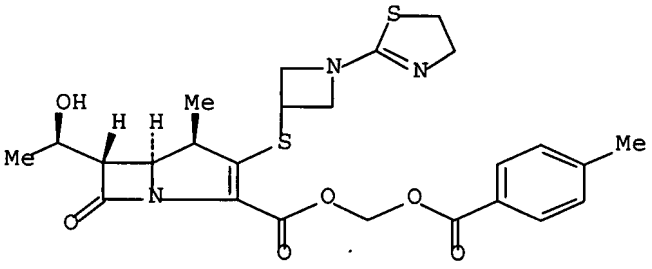
84%

CON: STEP(1) 5.5 hours, 100 deg C
STEP(2.1) 10 minutes, 5 deg C
STEP(2.2) 15 minutes
STEP(3.1) 2 hours, -20 deg C
STEP(3.2) 0.5 hours, 5 deg C
STEP(4.1) 1.5 hours, room temperature, 400 kPa
STEP(4.2) pH 5.6
STEP(5.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(5.2) 5 deg C, pH 4
STEP(5.3) pH 7.6

RX(75) OF 126 - 5 STEPS



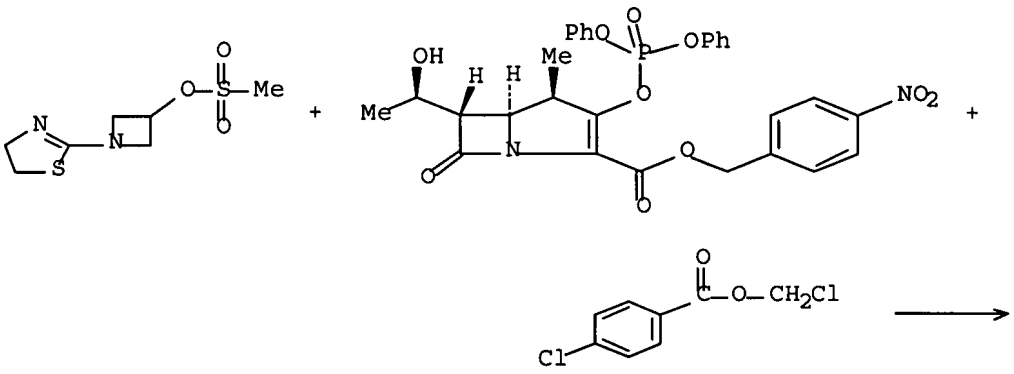
RX(75) OF 126 - 5 STEPS



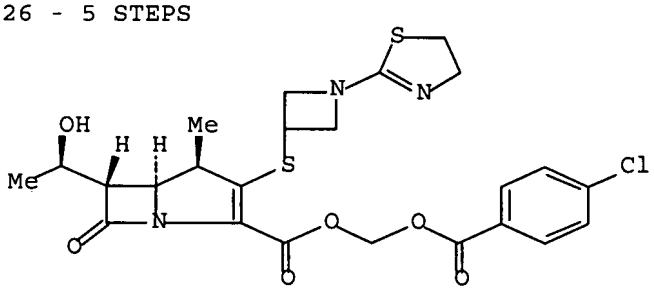
84%

CON: STEP(1) 5.5 hours, 100 deg C
STEP(2.1) 10 minutes, 5 deg C
STEP(2.2) 15 minutes
STEP(3.1) 2 hours, -20 deg C
STEP(3.2) 0.5 hours, 5 deg C
STEP(4.1) 1.5 hours, room temperature, 400 kPa
STEP(4.2) pH 5.6
STEP(5.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(5.2) 5 deg C, pH 4
STEP(5.3) pH 7.6

RX(76) OF 126 - 5 STEPS



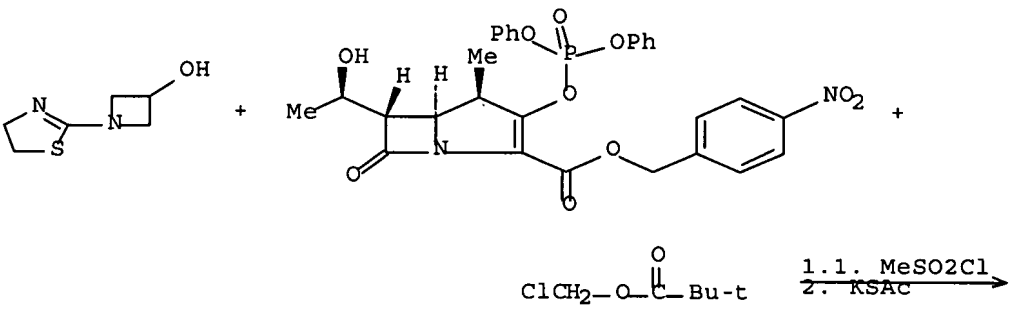
RX(76) OF 126 - 5 STEPS



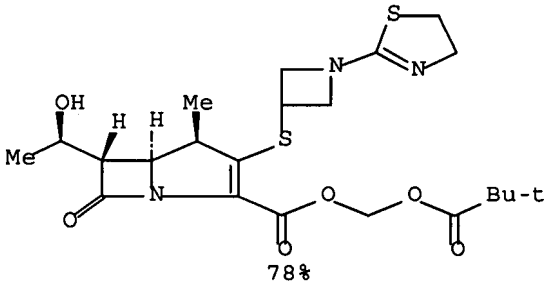
81%

CON: STEP(1) 5.5 hours, 100 deg C
STEP(2.1) 10 minutes, 5 deg C
STEP(2.2) 15 minutes
STEP(3.1) 2 hours, -20 deg C
STEP(3.2) 0.5 hours, 5 deg C
STEP(4.1) 1.5 hours, room temperature, 400 kPa
STEP(4.2) pH 5.6
STEP(5.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(5.2) 5 deg C, pH 4
STEP(5.3) pH 7.6

RX(77) OF 126 - 6 STEPS



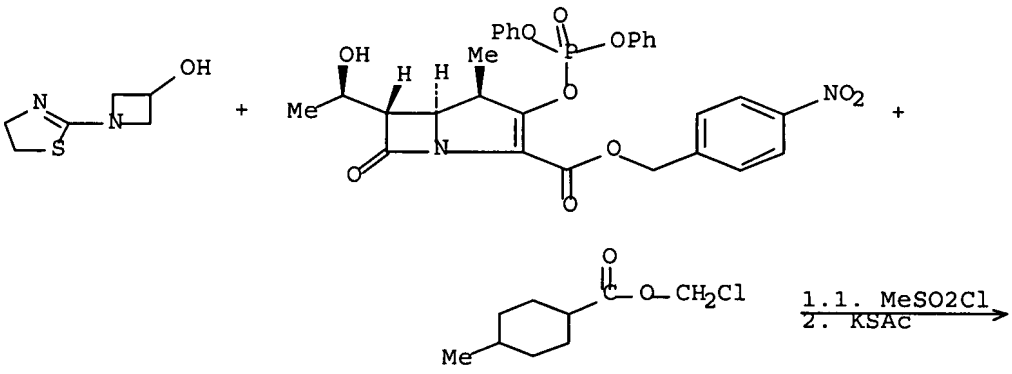
RX(77) OF 126 - 6 STEPS



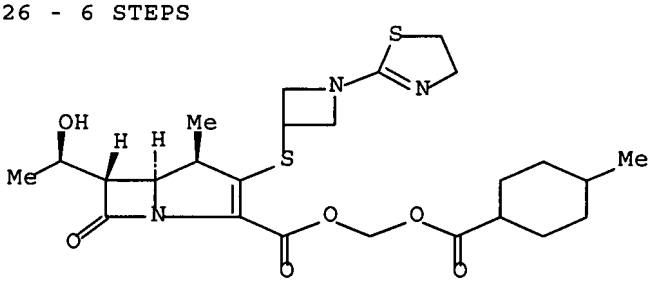
78%

CON: STEP(1.1) 0.5 hours, 5 deg C
STEP(1.2) 10 minutes, room temperature
STEP(2) 5.5 hours, 100 deg C
STEP(3.1) 10 minutes, 5 deg C
STEP(3.2) 15 minutes
STEP(4.1) 2 hours, -20 deg C
STEP(4.2) 0.5 hours, 5 deg C
STEP(5.1) 1.5 hours, room temperature, 400 kPa
STEP(5.2) pH 5.6
STEP(6.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(6.2) 5 deg C, pH 4
STEP(6.3) pH 7.6

RX(78) OF 126 - 6 STEPS



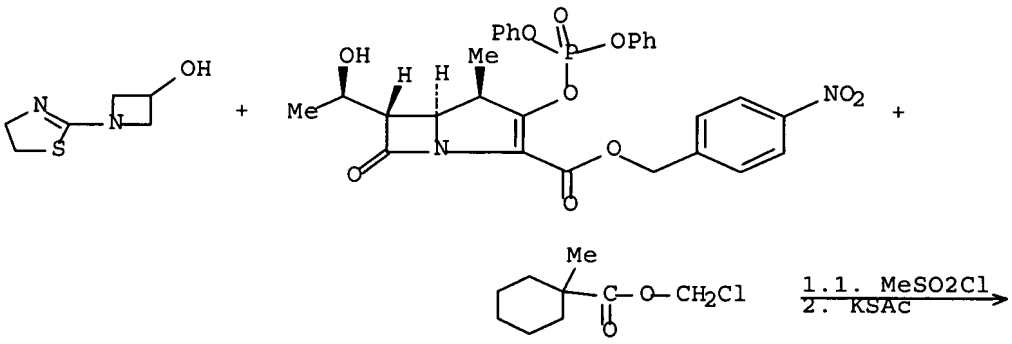
RX(78) OF 126 - 6 STEPS



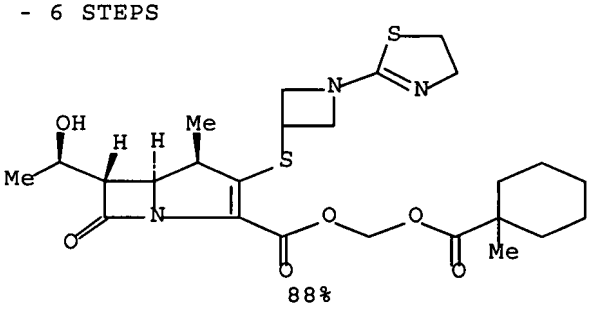
80%

CON: STEP(1.1) 0.5 hours, 5 deg C
STEP(1.2) 10 minutes, room temperature
STEP(2) 5.5 hours, 100 deg C
STEP(3.1) 10 minutes, 5 deg C
STEP(3.2) 15 minutes
STEP(4.1) 2 hours, -20 deg C
STEP(4.2) 0.5 hours, 5 deg C
STEP(5.1) 1.5 hours, room temperature, 400 kPa
STEP(5.2) pH 5.6
STEP(6.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(6.2) 5 deg C, pH 4
STEP(6.3) pH 7.6

RX(80) OF 126 - 6 STEPS

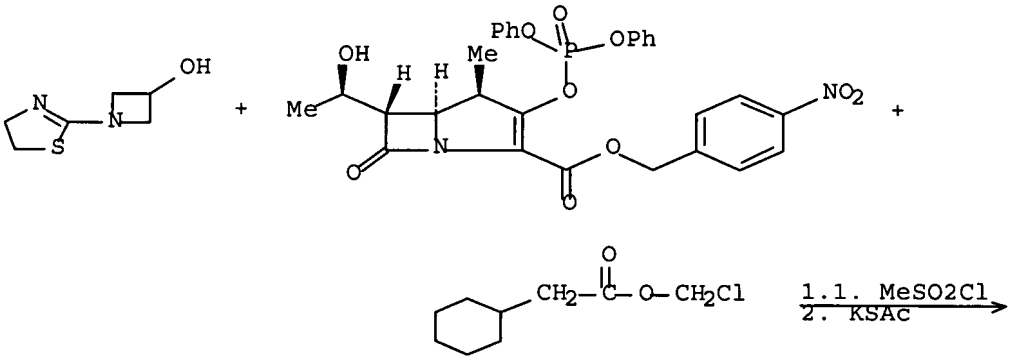


RX(80) OF 126 - 6 STEPS

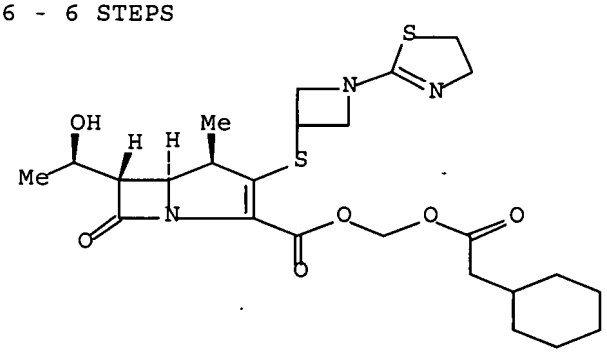


CON: STEP(1.1) 0.5 hours, 5 deg C
STEP(1.2) 10 minutes, room temperature
STEP(2) 5.5 hours, 100 deg C
STEP(3.1) 10 minutes, 5 deg C
STEP(3.2) 15 minutes
STEP(4.1) 2 hours, -20 deg C
STEP(4.2) 0.5 hours, 5 deg C
STEP(5.1) 1.5 hours, room temperature, 400 kPa
STEP(5.2) pH 5.6
STEP(6.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(6.2) 5 deg C, pH 4
STEP(6.3) pH 7.6

RX(81) OF 126 - 6 STEPS



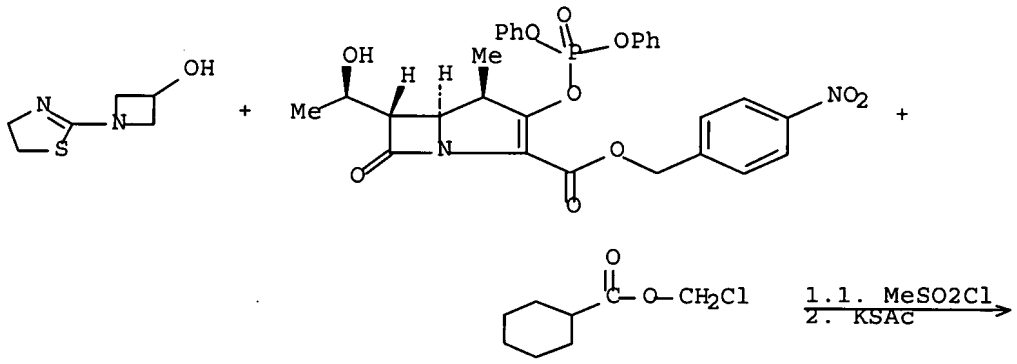
RX(81) OF 126 - 6 STEPS



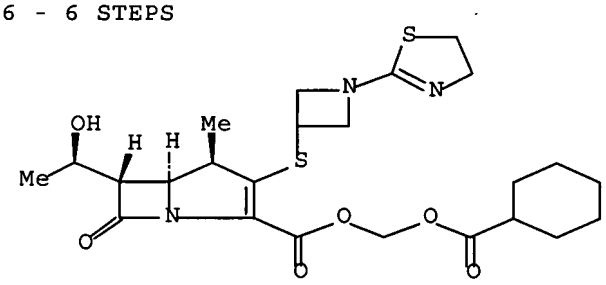
76%

CON: STEP(1.1) 0.5 hours, 5 deg C
STEP(1.2) 10 minutes, room temperature
STEP(2) 5.5 hours, 100 deg C
STEP(3.1) 10 minutes, 5 deg C
STEP(3.2) 15 minutes
STEP(4.1) 2 hours, -20 deg C
STEP(4.2) 0.5 hours, 5 deg C
STEP(5.1) 1.5 hours, room temperature, 400 kPa
STEP(5.2) pH 5.6
STEP(6.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(6.2) 5 deg C, pH 4
STEP(6.3) pH 7.6

RX(82) OF 126 - 6 STEPS



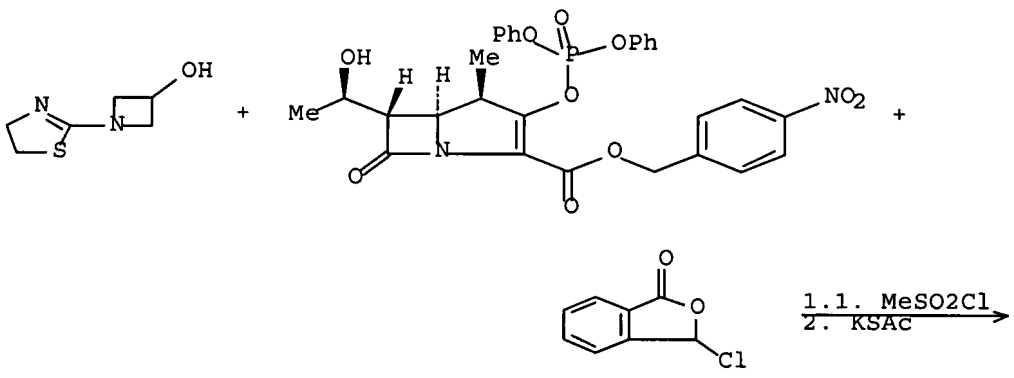
RX(82) OF 126 - 6 STEPS



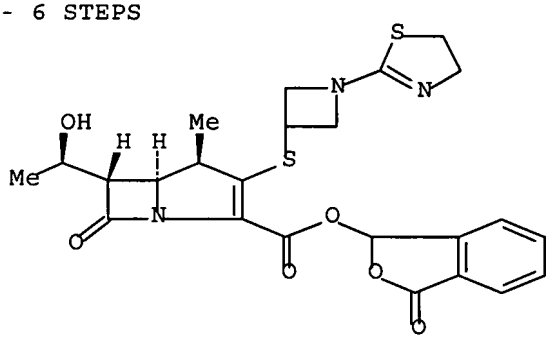
71%

CON: STEP(1.1) 0.5 hours, 5 deg C
STEP(1.2) 10 minutes, room temperature
STEP(2) 5.5 hours, 100 deg C
STEP(3.1) 10 minutes, 5 deg C
STEP(3.2) 15 minutes
STEP(4.1) 2 hours, -20 deg C
STEP(4.2) 0.5 hours, 5 deg C
STEP(5.1) 1.5 hours, room temperature, 400 kPa
STEP(5.2) pH 5.6
STEP(6.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(6.2) 5 deg C, pH 4
STEP(6.3) pH 7.6

RX(84) OF 126 - 6 STEPS



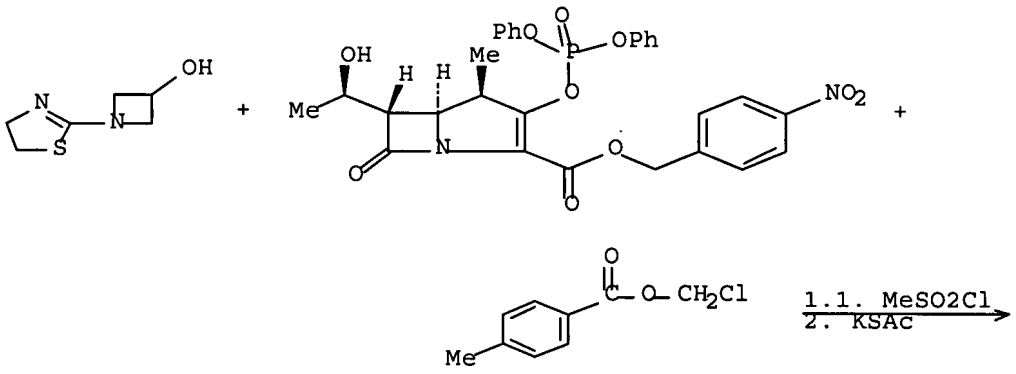
RX(84) OF 126 - 6 STEPS



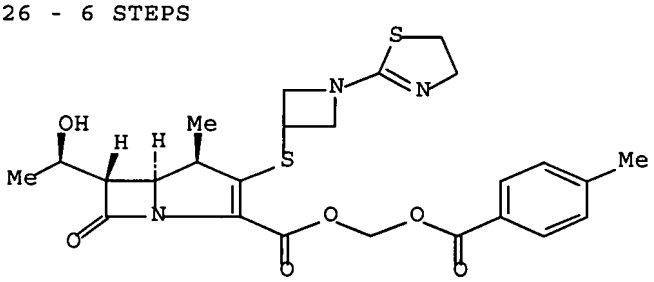
84%

CON: STEP(1.1) 0.5 hours, 5 deg C
STEP(1.2) 10 minutes, room temperature
STEP(2) 5.5 hours, 100 deg C
STEP(3.1) 10 minutes, 5 deg C
STEP(3.2) 15 minutes
STEP(4.1) 2 hours, -20 deg C
STEP(4.2) 0.5 hours, 5 deg C
STEP(5.1) 1.5 hours, room temperature, 400 kPa
STEP(5.2) pH 5.6
STEP(6.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(6.2) 5 deg C, pH 4
STEP(6.3) pH 7.6

RX(85) OF 126 - 6 STEPS



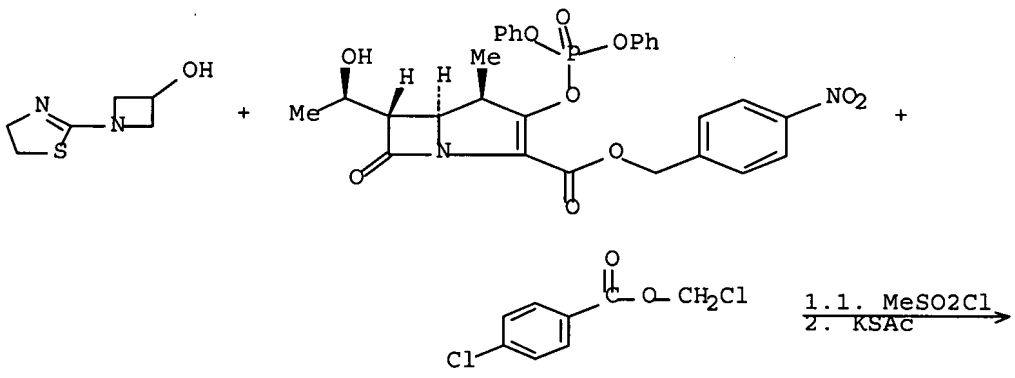
RX(85) OF 126 - 6 STEPS



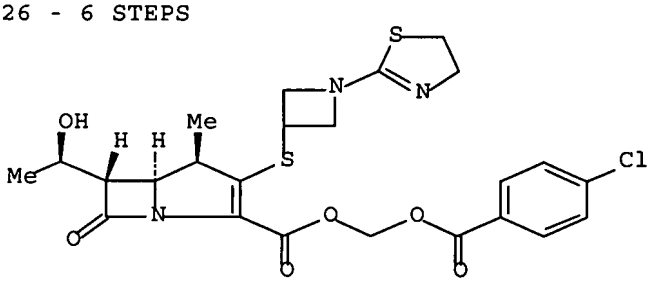
84%

CON: STEP(1.1) 0.5 hours, 5 deg C
STEP(1.2) 10 minutes, room temperature
STEP(2) 5.5 hours, 100 deg C
STEP(3.1) 10 minutes, 5 deg C
STEP(3.2) 15 minutes
STEP(4.1) 2 hours, -20 deg C
STEP(4.2) 0.5 hours, 5 deg C
STEP(5.1) 1.5 hours, room temperature, 400 kPa
STEP(5.2) pH 5.6
STEP(6.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(6.2) 5 deg C, pH 4
STEP(6.3) pH 7.6

RX(86) OF 126 - 6 STEPS



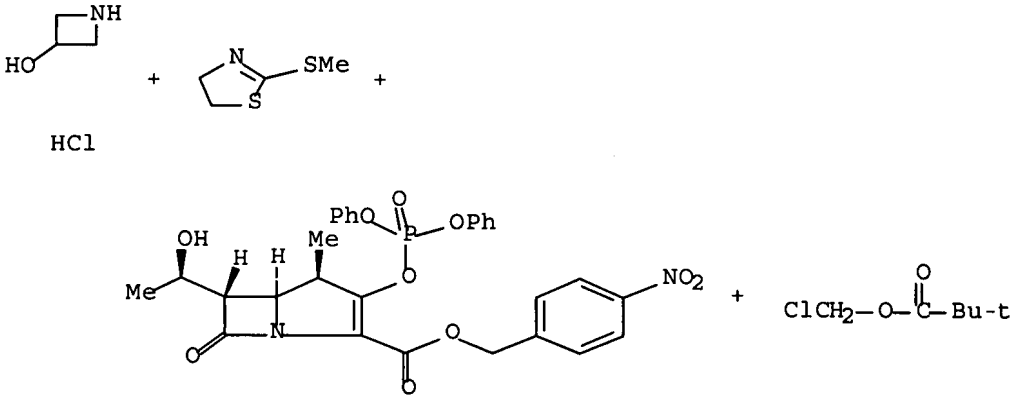
RX(86) OF 126 - 6 STEPS



81%

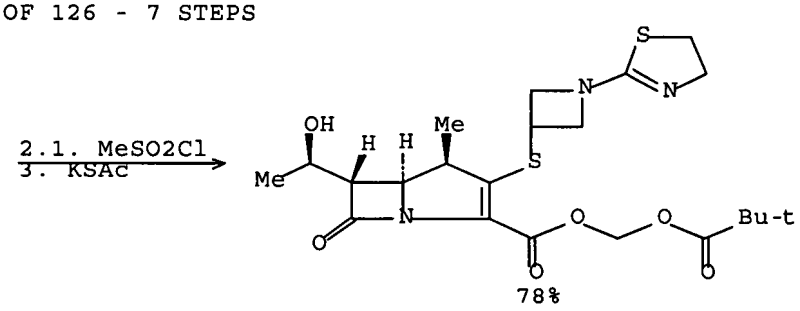
CON: STEP(1.1) 0.5 hours, 5 deg C
STEP(1.2) 10 minutes, room temperature
STEP(2) 5.5 hours, 100 deg C
STEP(3.1) 10 minutes, 5 deg C
STEP(3.2) 15 minutes
STEP(4.1) 2 hours, -20 deg C
STEP(4.2) 0.5 hours, 5 deg C
STEP(5.1) 1.5 hours, room temperature, 400 kPa
STEP(5.2) pH 5.6
STEP(6.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(6.2) 5 deg C, pH 4
STEP(6.3) pH 7.6

RX(87) OF 126 - 7 STEPS



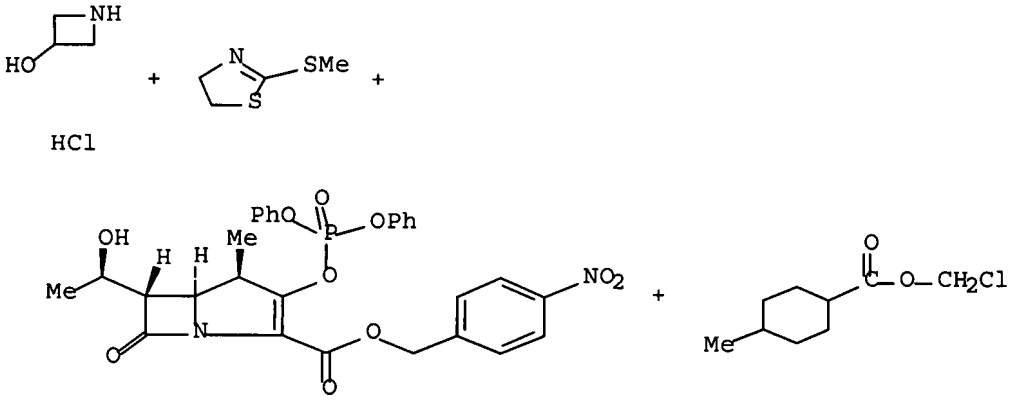
HCl

RX(87) OF 126 - 7 STEPS

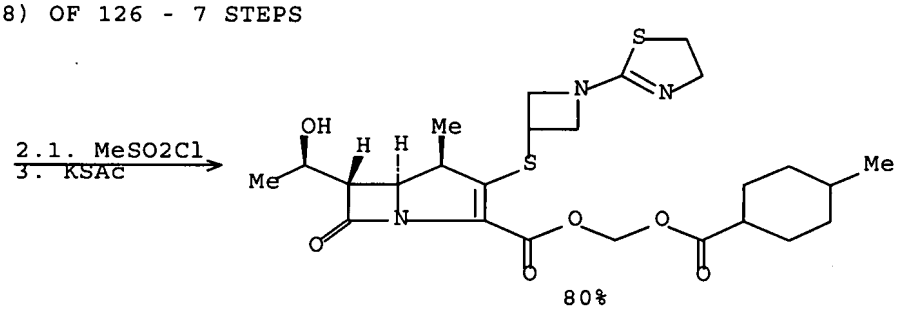


CON: STEP(1.1) 23 hours, reflux; reflux -> 40 deg C
STEP(1.2) 2 hours, 40 deg C
STEP(2.1) 0.5 hours, 5 deg C
STEP(2.2) 10 minutes, room temperature
STEP(3) 5.5 hours, 100 deg C
STEP(4.1) 10 minutes, 5 deg C
STEP(4.2) 15 minutes
STEP(5.1) 2 hours, -20 deg C
STEP(5.2) 0.5 hours, 5 deg C
STEP(6.1) 1.5 hours, room temperature, 400 kPa
STEP(6.2) pH 5.6
STEP(7.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(7.2) 5 deg C, pH 4
STEP(7.3) pH 7.6

RX(88) OF 126 - 7 STEPS

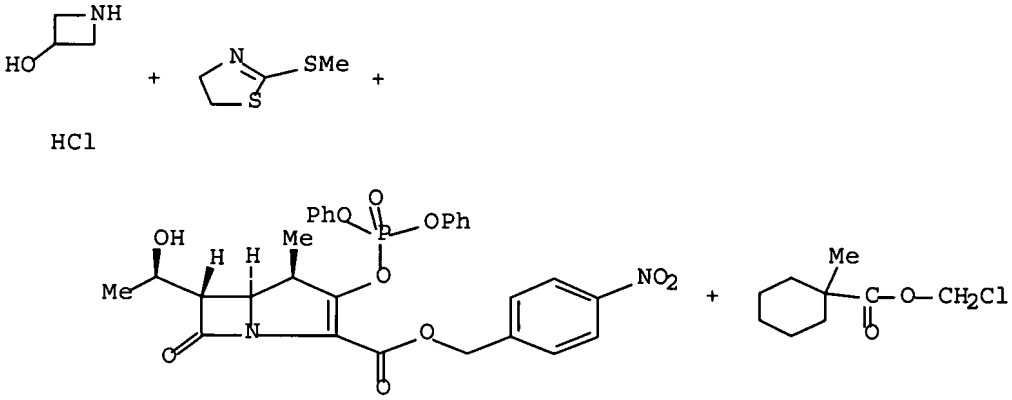


RX(88) OF 126 - 7 STEPS

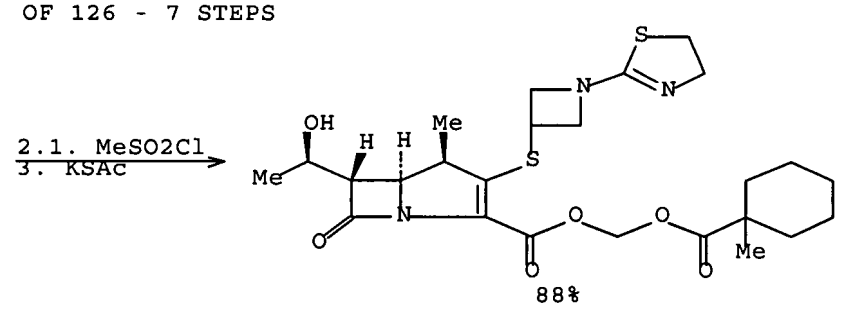


CON: STEP(1.1) 23 hours, reflux; reflux -> 40 deg C
STEP(1.2) 2 hours, 40 deg C
STEP(2.1) 0.5 hours, 5 deg C
STEP(2.2) 10 minutes, room temperature
STEP(3) 5.5 hours, 100 deg C
STEP(4.1) 10 minutes, 5 deg C
STEP(4.2) 15 minutes
STEP(5.1) 2 hours, -20 deg C
STEP(5.2) 0.5 hours, 5 deg C
STEP(6.1) 1.5 hours, room temperature, 400 kPa
STEP(6.2) pH 5.6
STEP(7.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(7.2) 5 deg C, pH 4
STEP(7.3) pH 7.6

RX(90) OF 126 - 7 STEPS

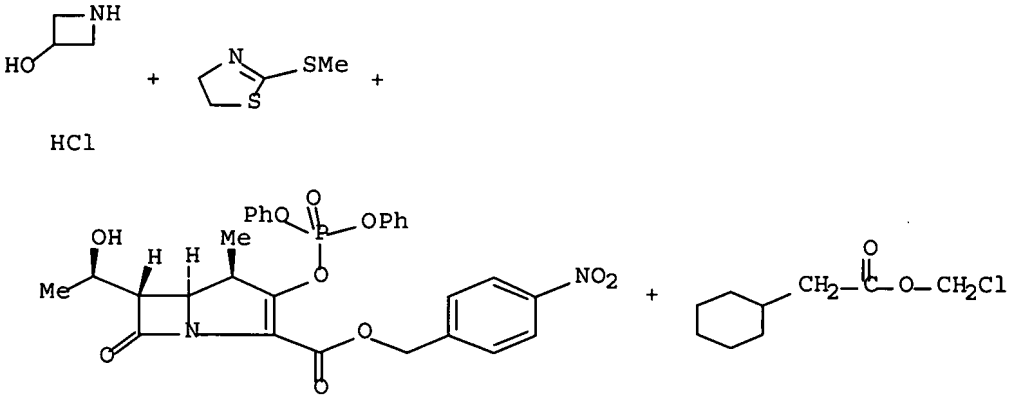


RX(90) OF 126 - 7 STEPS

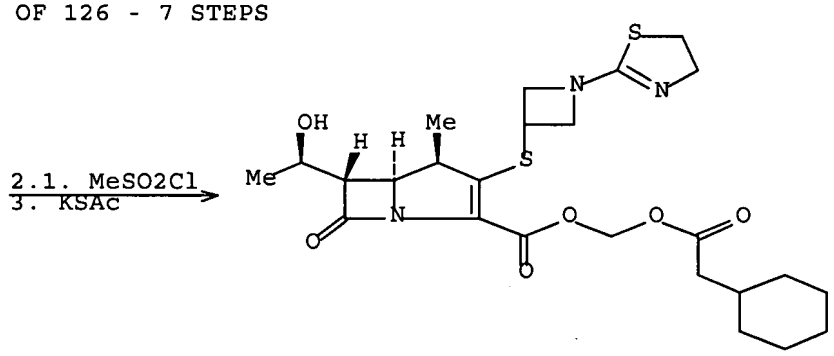


CON: STEP(1.1) 23 hours, reflux; reflux -> 40 deg C
STEP(1.2) 2 hours, 40 deg C
STEP(2.1) 0.5 hours, 5 deg C
STEP(2.2) 10 minutes, room temperature
STEP(3) 5.5 hours, 100 deg C
STEP(4.1) 10 minutes, 5 deg C
STEP(4.2) 15 minutes
STEP(5.1) 2 hours, -20 deg C
STEP(5.2) 0.5 hours, 5 deg C
STEP(6.1) 1.5 hours, room temperature, 400 kPa
STEP(6.2) pH 5.6
STEP(7.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(7.2) 5 deg C, pH 4
STEP(7.3) pH 7.6

RX(91) OF 126 - 7 STEPS



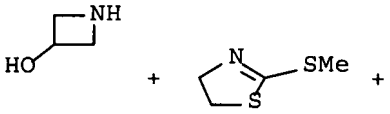
RX(91) OF 126 - 7 STEPS



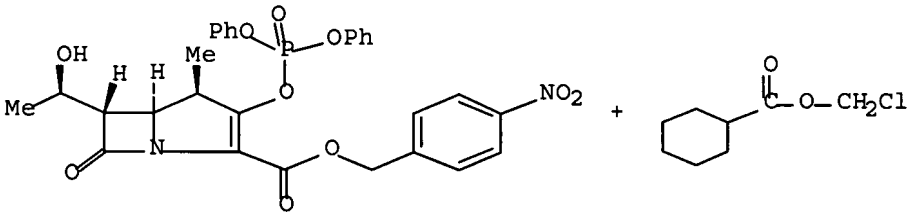
76%

CON: STEP(1.1) 23 hours, reflux; reflux -> 40 deg C
STEP(1.2) 2 hours, 40 deg C
STEP(2.1) 0.5 hours, 5 deg C
STEP(2.2) 10 minutes, room temperature
STEP(3) 5.5 hours, 100 deg C
STEP(4.1) 10 minutes, 5 deg C
STEP(4.2) 15 minutes
STEP(5.1) 2 hours, -20 deg C
STEP(5.2) 0.5 hours, 5 deg C
STEP(6.1) 1.5 hours, room temperature, 400 kPa
STEP(6.2) pH 5.6
STEP(7.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(7.2) 5 deg C, pH 4
STEP(7.3) pH 7.6

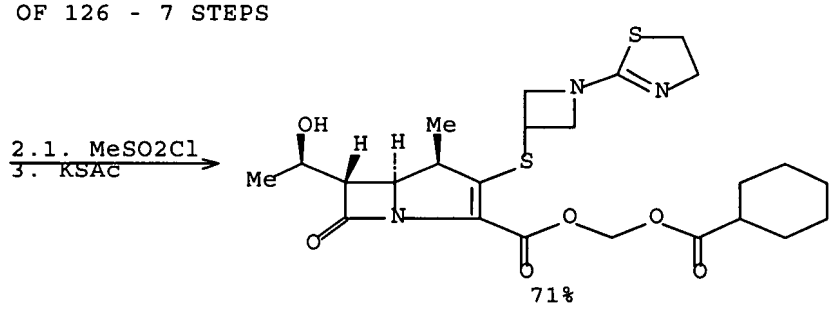
RX(92) OF 126 - 7 STEPS



HCl

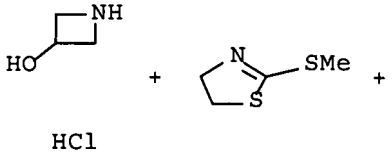


RX(92) OF 126 - 7 STEPS

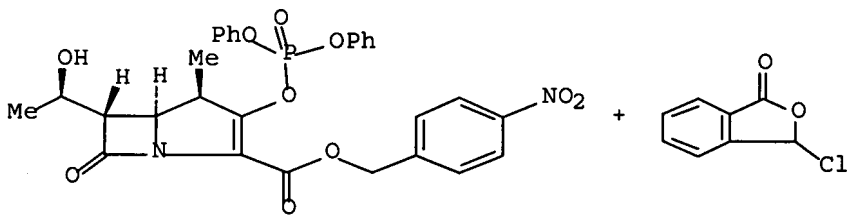


CON: STEP(1.1) 23 hours, reflux; reflux -> 40 deg C
STEP(1.2) 2 hours, 40 deg C
STEP(2.1) 0.5 hours, 5 deg C
STEP(2.2) 10 minutes, room temperature
STEP(3) 5.5 hours, 100 deg C
STEP(4.1) 10 minutes, 5 deg C
STEP(4.2) 15 minutes
STEP(5.1) 2 hours, -20 deg C
STEP(5.2) 0.5 hours, 5 deg C
STEP(6.1) 1.5 hours, room temperature, 400 kPa
STEP(6.2) pH 5.6
STEP(7.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(7.2) 5 deg C, pH 4
STEP(7.3) pH 7.6

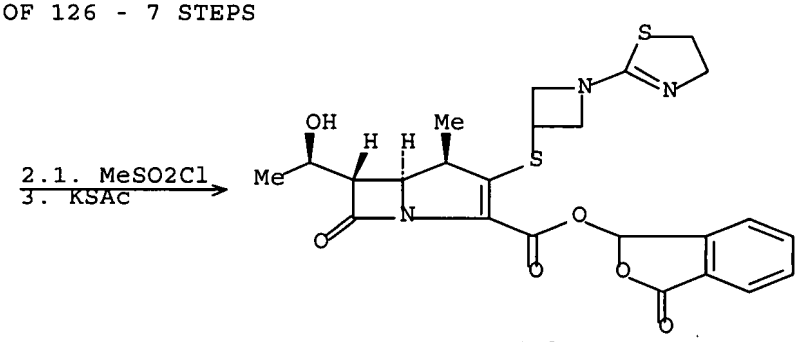
RX(94) OF 126 - 7 STEPS



HCl



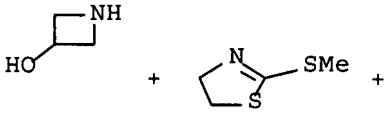
RX(94) OF 126 - 7 STEPS



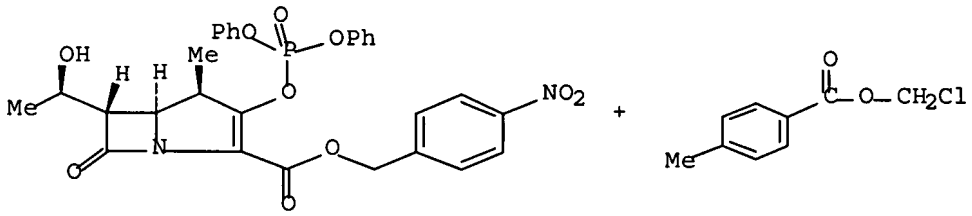
84%

CON: STEP(1.1) 23 hours, reflux; reflux -> 40 deg C
STEP(1.2) 2 hours, 40 deg C
STEP(2.1) 0.5 hours, 5 deg C
STEP(2.2) 10 minutes, room temperature
STEP(3) 5.5 hours, 100 deg C
STEP(4.1) 10 minutes, 5 deg C
STEP(4.2) 15 minutes
STEP(5.1) 2 hours, -20 deg C
STEP(5.2) 0.5 hours, 5 deg C
STEP(6.1) 1.5 hours, room temperature, 400 kPa
STEP(6.2) pH 5.6
STEP(7.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(7.2) 5 deg C, pH 4
STEP(7.3) pH 7.6

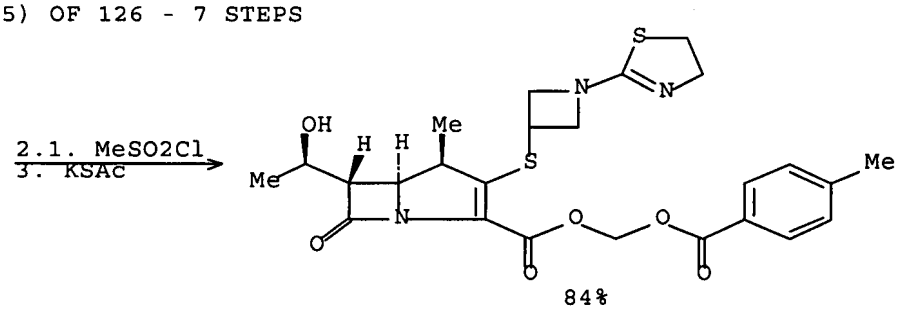
RX(95) OF 126 - 7 STEPS



HCl



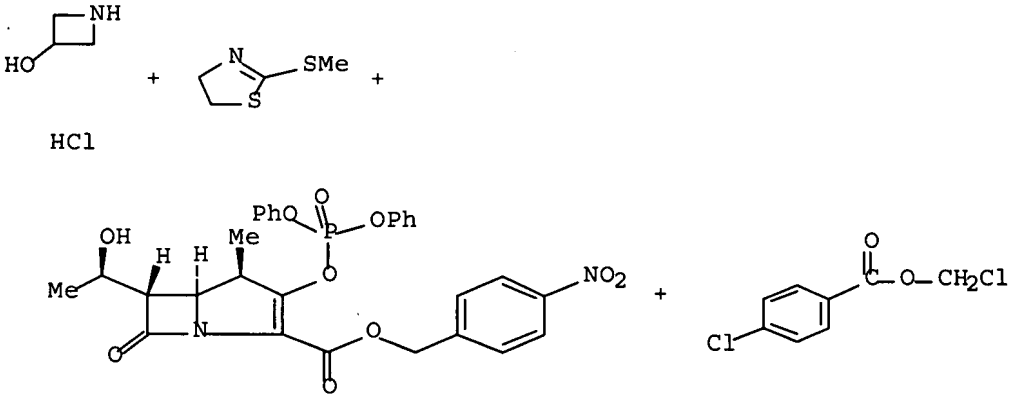
RX(95) OF 126 - 7 STEPS



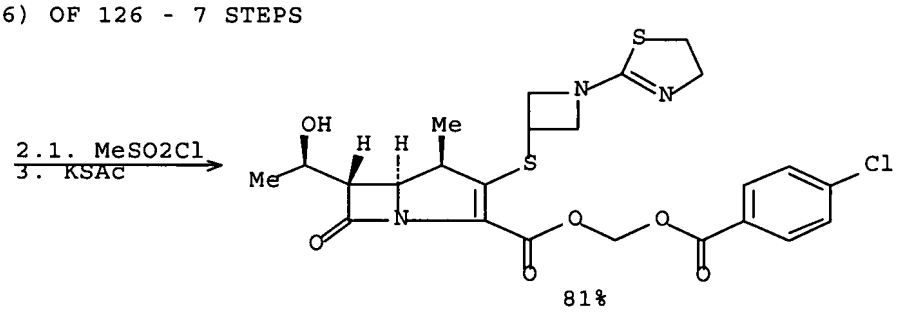
84%

CON: STEP(1.1) 23 hours, reflux; reflux -> 40 deg C
STEP(1.2) 2 hours, 40 deg C
STEP(2.1) 0.5 hours, 5 deg C
STEP(2.2) 10 minutes, room temperature
STEP(3) 5.5 hours, 100 deg C
STEP(4.1) 10 minutes, 5 deg C
STEP(4.2) 15 minutes
STEP(5.1) 2 hours, -20 deg C
STEP(5.2) 0.5 hours, 5 deg C
STEP(6.1) 1.5 hours, room temperature, 400 kPa
STEP(6.2) pH 5.6
STEP(7.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(7.2) 5 deg C, pH 4
STEP(7.3) pH 7.6

RX(96) OF 126 - 7 STEPS

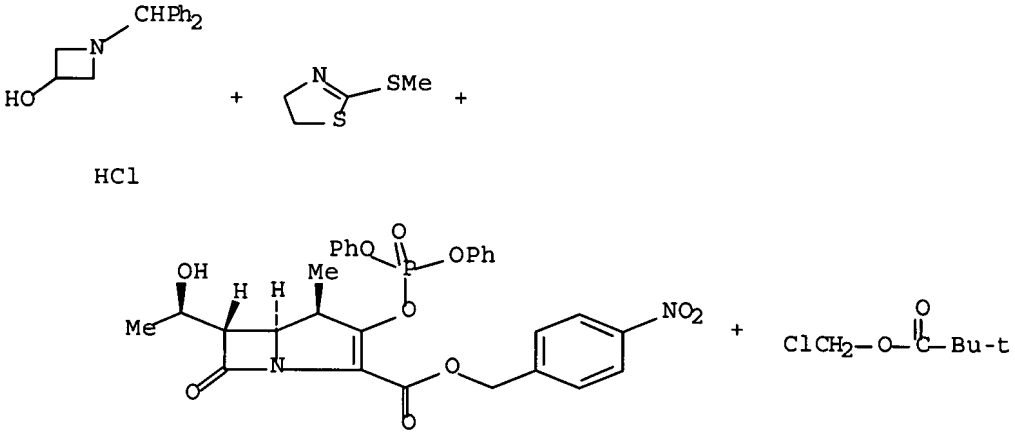


RX(96) OF 126 - 7 STEPS

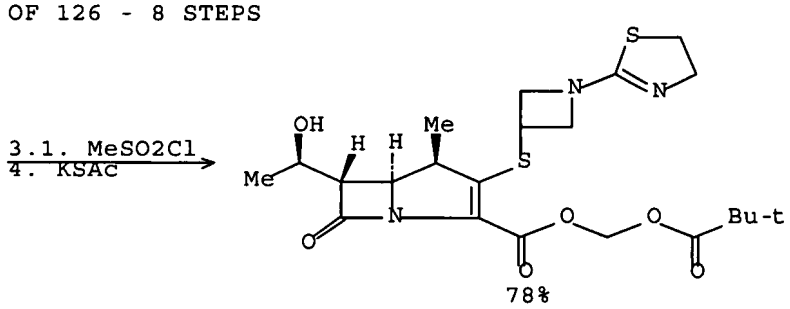


CON: STEP(1.1) 23 hours, reflux; reflux -> 40 deg C
STEP(1.2) 2 hours, 40 deg C
STEP(2.1) 0.5 hours, 5 deg C
STEP(2.2) 10 minutes, room temperature
STEP(3) 5.5 hours, 100 deg C
STEP(4.1) 10 minutes, 5 deg C
STEP(4.2) 15 minutes
STEP(5.1) 2 hours, -20 deg C
STEP(5.2) 0.5 hours, 5 deg C
STEP(6.1) 1.5 hours, room temperature, 400 kPa
STEP(6.2) pH 5.6
STEP(7.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(7.2) 5 deg C, pH 4
STEP(7.3) pH 7.6

RX(107) OF 126 - 8 STEPS

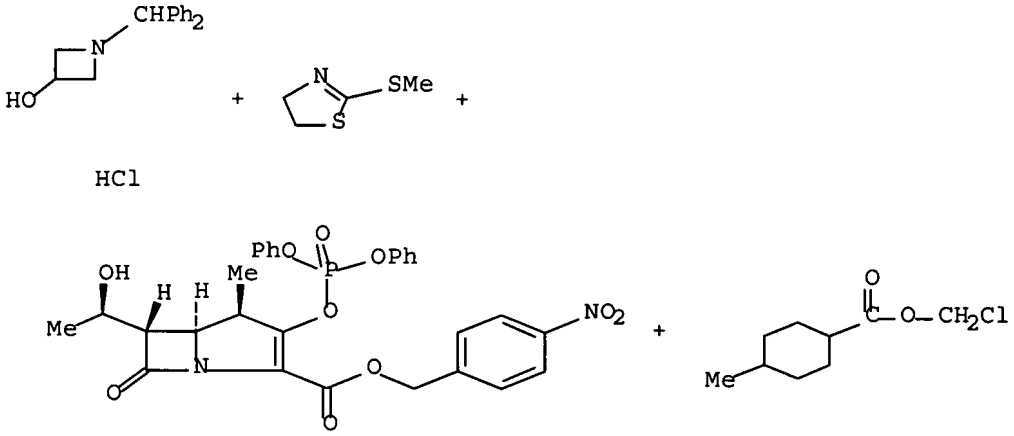


RX(107) OF 126 - 8 STEPS

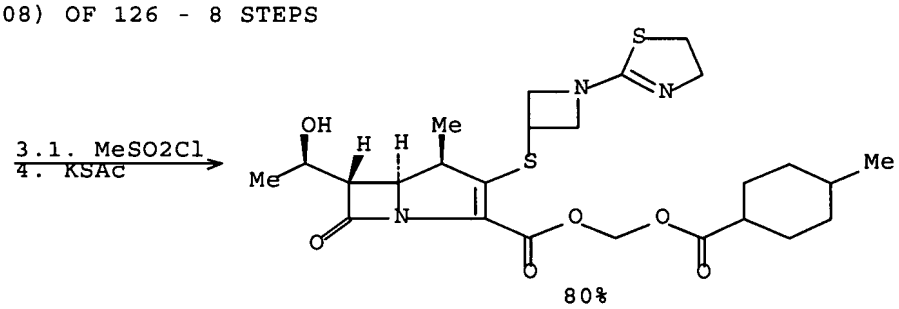


CON: STEP(1.1) 4 hours, room temperature, 350 kPa
STEP(2.1) 23 hours, reflux; reflux -> 40 deg C
STEP(2.2) 2 hours, 40 deg C
STEP(3.1) 0.5 hours, 5 deg C
STEP(3.2) 10 minutes, room temperature
STEP(4) 5.5 hours, 100 deg C
STEP(5.1) 10 minutes, 5 deg C
STEP(5.2) 15 minutes
STEP(6.1) 2 hours, -20 deg C
STEP(6.2) 0.5 hours, 5 deg C
STEP(7.1) 1.5 hours, room temperature, 400 kPa
STEP(7.2) pH 5.6
STEP(8.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(8.2) 5 deg C, pH 4
STEP(8.3) pH 7.6

RX(108) OF 126 - 8 STEPS

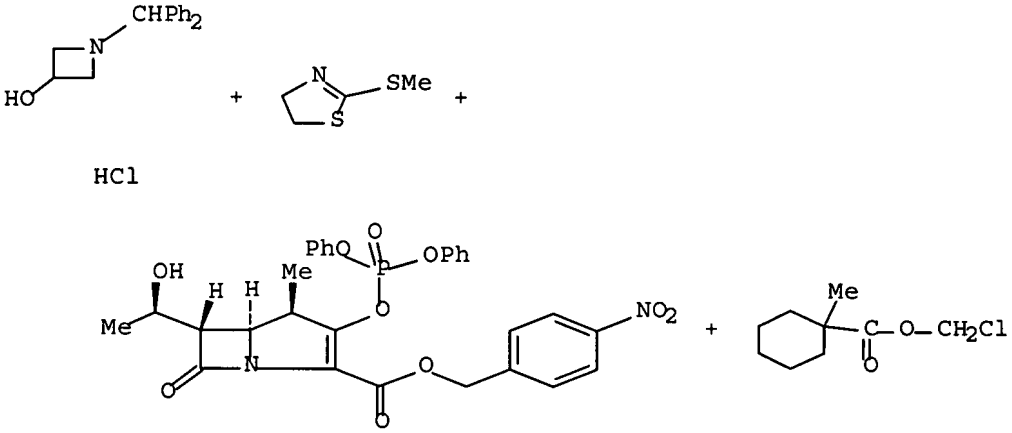


RX(108) OF 126 - 8 STEPS

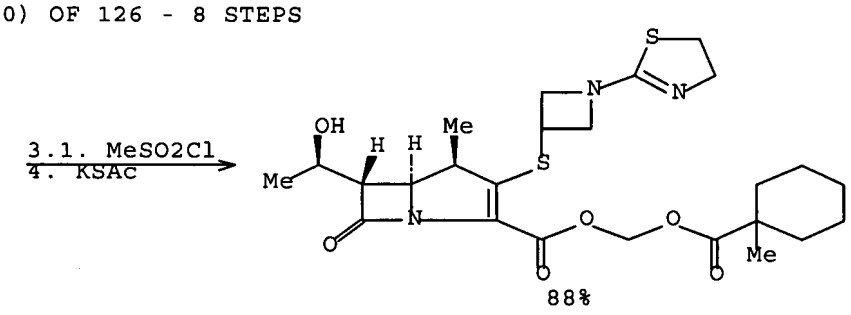


CON: STEP(1.1) 4 hours, room temperature, 350 kPa
STEP(2.1) 23 hours, reflux; reflux -> 40 deg C
STEP(2.2) 2 hours, 40 deg C
STEP(3.1) 0.5 hours, 5 deg C
STEP(3.2) 10 minutes, room temperature
STEP(4) 5.5 hours, 100 deg C
STEP(5.1) 10 minutes, 5 deg C
STEP(5.2) 15 minutes
STEP(6.1) 2 hours, -20 deg C
STEP(6.2) 0.5 hours, 5 deg C
STEP(7.1) 1.5 hours, room temperature, 400 kPa
STEP(7.2) pH 5.6
STEP(8.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(8.2) 5 deg C, pH 4
STEP(8.3) pH 7.6

RX(110) OF 126 - 8 STEPS

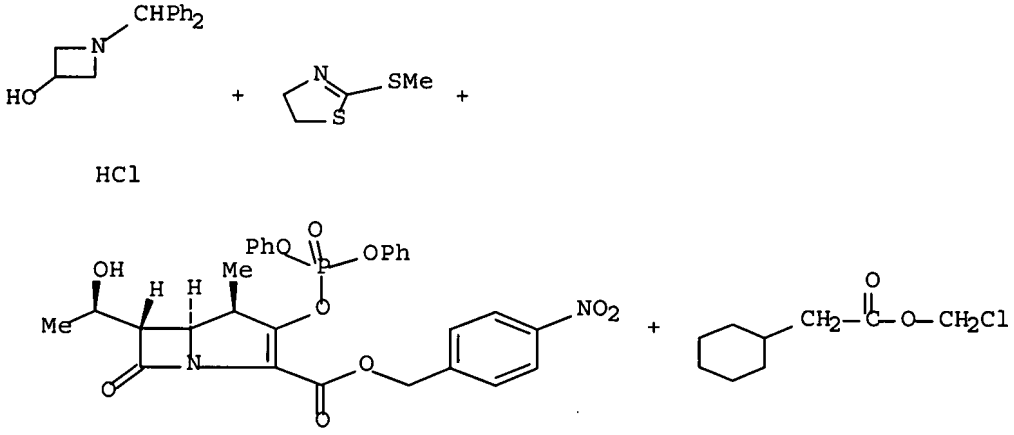


RX(110) OF 126 - 8 STEPS

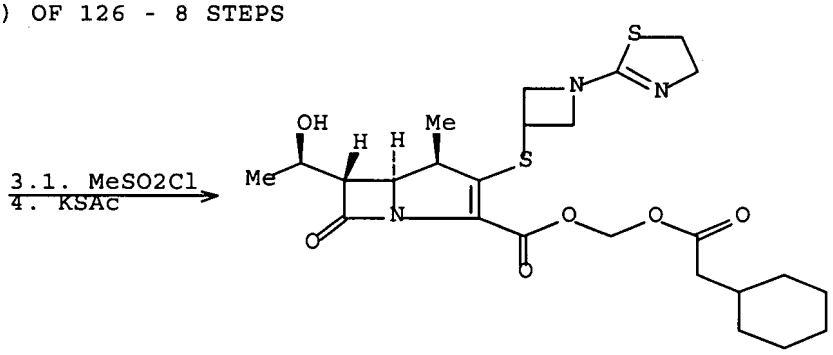


CON: STEP(1.1) 4 hours, room temperature, 350 kPa
STEP(2.1) 23 hours, reflux; reflux -> 40 deg C
STEP(2.2) 2 hours, 40 deg C
STEP(3.1) 0.5 hours, 5 deg C
STEP(3.2) 10 minutes, room temperature
STEP(4) 5.5 hours, 100 deg C
STEP(5.1) 10 minutes, 5 deg C
STEP(5.2) 15 minutes
STEP(6.1) 2 hours, -20 deg C
STEP(6.2) 0.5 hours, 5 deg C
STEP(7.1) 1.5 hours, room temperature, 400 kPa
STEP(7.2) pH 5.6
STEP(8.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(8.2) 5 deg C, pH 4
STEP(8.3) pH 7.6

RX(111) OF 126 - 8 STEPS



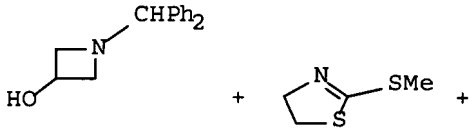
RX(111) OF 126 - 8 STEPS



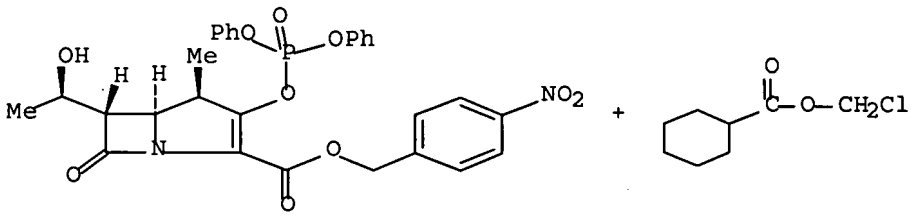
76%

CON: STEP(1.1) 4 hours, room temperature, 350 kPa
STEP(2.1) 23 hours, reflux; reflux -> 40 deg C
STEP(2.2) 2 hours, 40 deg C
STEP(3.1) 0.5 hours, 5 deg C
STEP(3.2) 10 minutes, room temperature
STEP(4) 5.5 hours, 100 deg C
STEP(5.1) 10 minutes, 5 deg C
STEP(5.2) 15 minutes
STEP(6.1) 2 hours, -20 deg C
STEP(6.2) 0.5 hours, 5 deg C
STEP(7.1) 1.5 hours, room temperature, 400 kPa
STEP(7.2) pH 5.6
STEP(8.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(8.2) 5 deg C, pH 4
STEP(8.3) pH 7.6

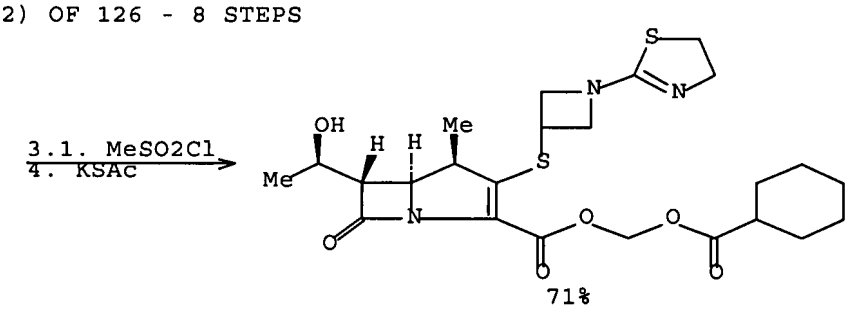
RX(112) OF 126 - 8 STEPS



HCl

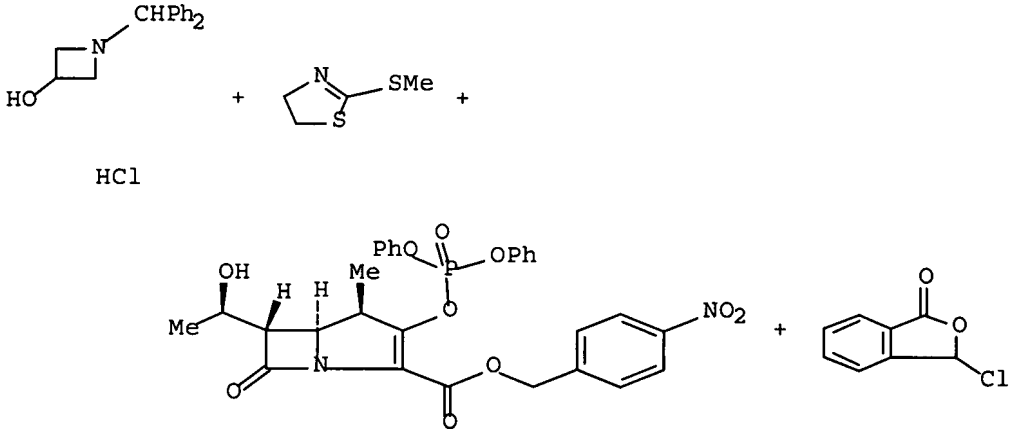


RX(112) OF 126 - 8 STEPS

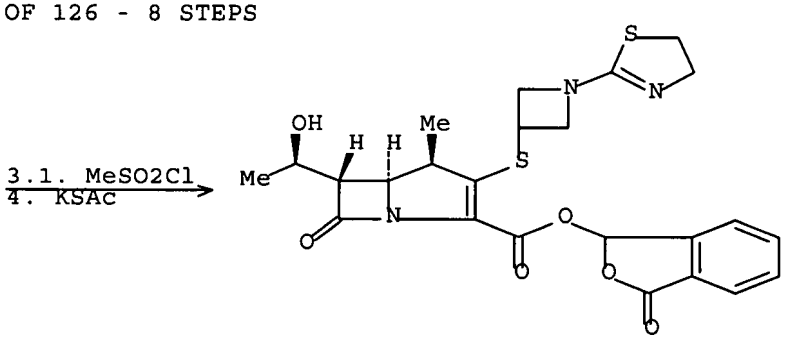


CON: STEP(1.1) 4 hours, room temperature, 350 kPa
STEP(2.1) 23 hours, reflux; reflux -> 40 deg C
STEP(2.2) 2 hours, 40 deg C
STEP(3.1) 0.5 hours, 5 deg C
STEP(3.2) 10 minutes, room temperature
STEP(4) 5.5 hours, 100 deg C
STEP(5.1) 10 minutes, 5 deg C
STEP(5.2) 15 minutes
STEP(6.1) 2 hours, -20 deg C
STEP(6.2) 0.5 hours, 5 deg C
STEP(7.1) 1.5 hours, room temperature, 400 kPa
STEP(7.2) pH 5.6
STEP(8.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(8.2) 5 deg C, pH 4
STEP(8.3) pH 7.6

RX(114) OF 126 - 8 STEPS



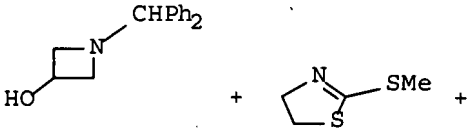
RX(114) OF 126 - 8 STEPS



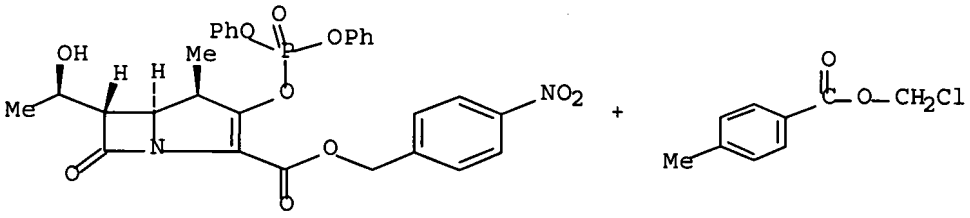
84%

CON: STEP(1.1) 4 hours, room temperature, 350 kPa
STEP(2.1) 23 hours, reflux; reflux -> 40 deg C
STEP(2.2) 2 hours, 40 deg C
STEP(3.1) 0.5 hours, 5 deg C
STEP(3.2) 10 minutes, room temperature
STEP(4) 5.5 hours, 100 deg C
STEP(5.1) 10 minutes, 5 deg C
STEP(5.2) 15 minutes
STEP(6.1) 2 hours, -20 deg C
STEP(6.2) 0.5 hours, 5 deg C
STEP(7.1) 1.5 hours, room temperature, 400 kPa
STEP(7.2) pH 5.6
STEP(8.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(8.2) 5 deg C, pH 4
STEP(8.3) pH 7.6

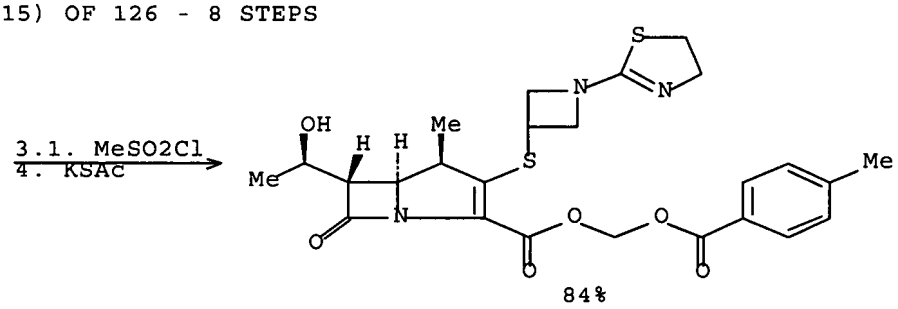
RX(115) OF 126 - 8 STEPS



HCl

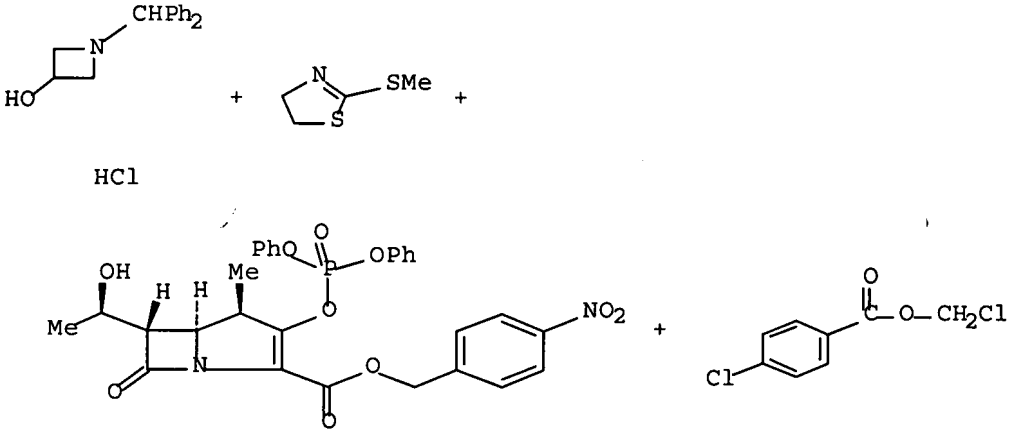


RX(115) OF 126 - 8 STEPS

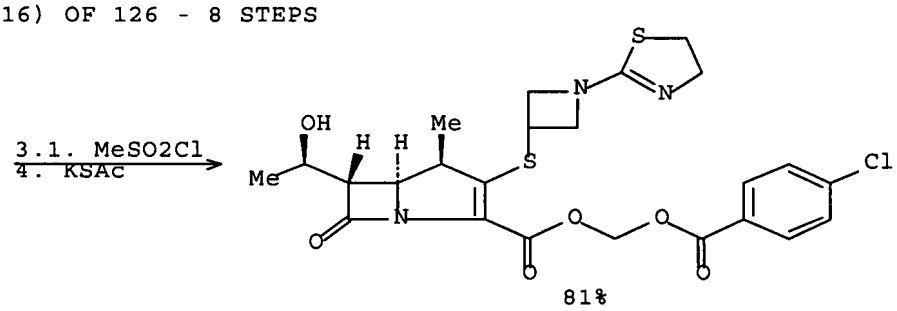


CON: STEP(1.1) 4 hours, room temperature, 350 kPa
STEP(2.1) 23 hours, reflux; reflux -> 40 deg C
STEP(2.2) 2 hours, 40 deg C
STEP(3.1) 0.5 hours, 5 deg C
STEP(3.2) 10 minutes, room temperature
STEP(4) 5.5 hours, 100 deg C
STEP(5.1) 10 minutes, 5 deg C
STEP(5.2) 15 minutes
STEP(6.1) 2 hours, -20 deg C
STEP(6.2) 0.5 hours, 5 deg C
STEP(7.1) 1.5 hours, room temperature, 400 kPa
STEP(7.2) pH 5.6
STEP(8.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(8.2) 5 deg C, pH 4
STEP(8.3) pH 7.6

RX(116) OF 126 - 8 STEPS



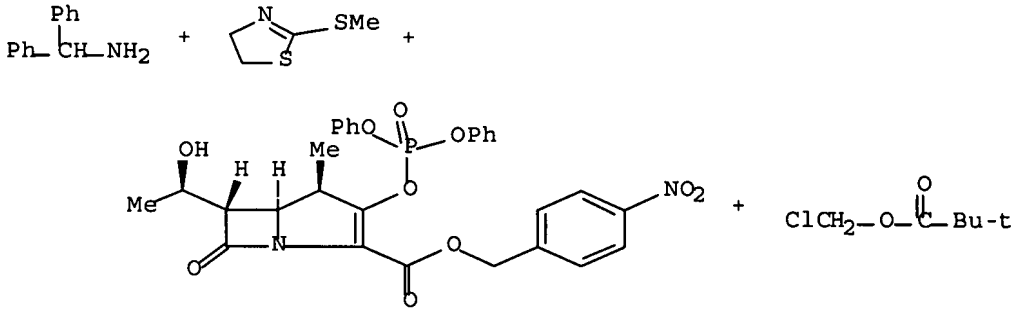
RX(116) OF 126 - 8 STEPS



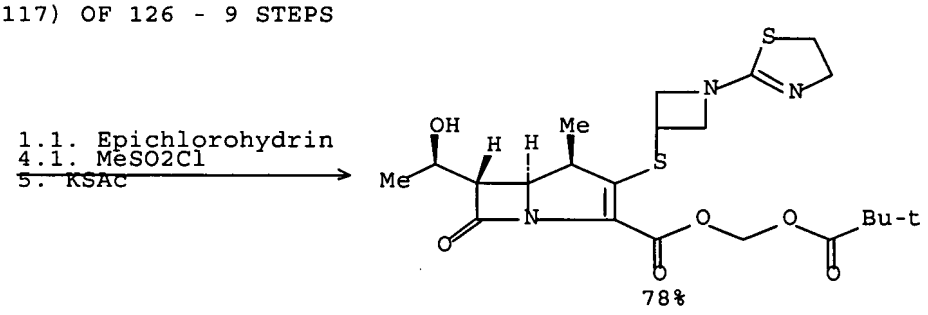
81%

CON: STEP(1.1) 4 hours, room temperature, 350 kPa
STEP(2.1) 23 hours, reflux; reflux -> 40 deg C
STEP(2.2) 2 hours, 40 deg C
STEP(3.1) 0.5 hours, 5 deg C
STEP(3.2) 10 minutes, room temperature
STEP(4) 5.5 hours, 100 deg C
STEP(5.1) 10 minutes, 5 deg C
STEP(5.2) 15 minutes
STEP(6.1) 2 hours, -20 deg C
STEP(6.2) 0.5 hours, 5 deg C
STEP(7.1) 1.5 hours, room temperature, 400 kPa
STEP(7.2) pH 5.6
STEP(8.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(8.2) 5 deg C, pH 4
STEP(8.3) pH 7.6

RX(117) OF 126 - 9 STEPS

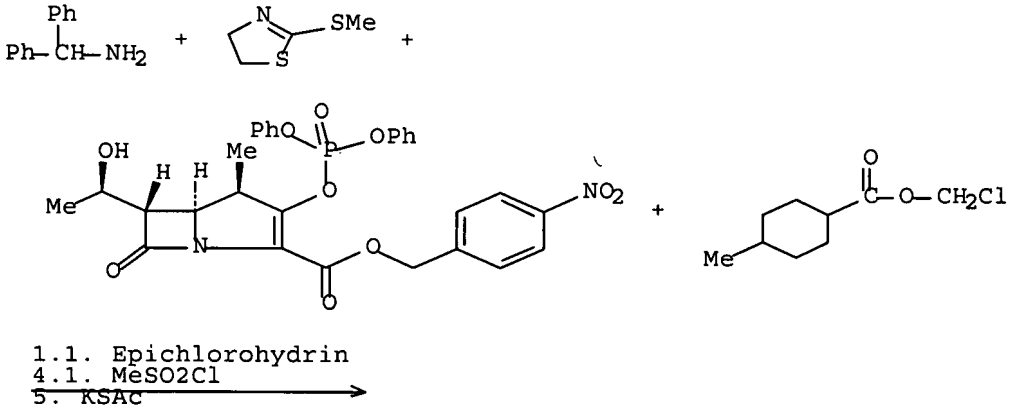


RX(117) OF 126 - 9 STEPS

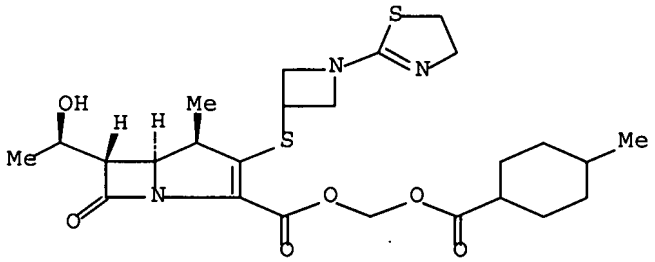


CON: STEP(1.1) 1 day, room temperature
STEP(1.2) 3 days, 50 deg C
STEP(2.1) 4 hours, room temperature, 350 kPa
STEP(3.1) 23 hours, reflux; reflux -> 40 deg C
STEP(3.2) 2 hours, 40 deg C
STEP(4.1) 0.5 hours, 5 deg C
STEP(4.2) 10 minutes, room temperature
STEP(5) 5.5 hours, 100 deg C
STEP(6.1) 10 minutes, 5 deg C
STEP(6.2) 15 minutes
STEP(7.1) 2 hours, -20 deg C
STEP(7.2) 0.5 hours, 5 deg C
STEP(8.1) 1.5 hours, room temperature, 400 kPa
STEP(8.2) pH 5.6
STEP(9.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(9.2) 5 deg C, pH 4
STEP(9.3) pH 7.6

RX(118) OF 126 - 9 STEPS



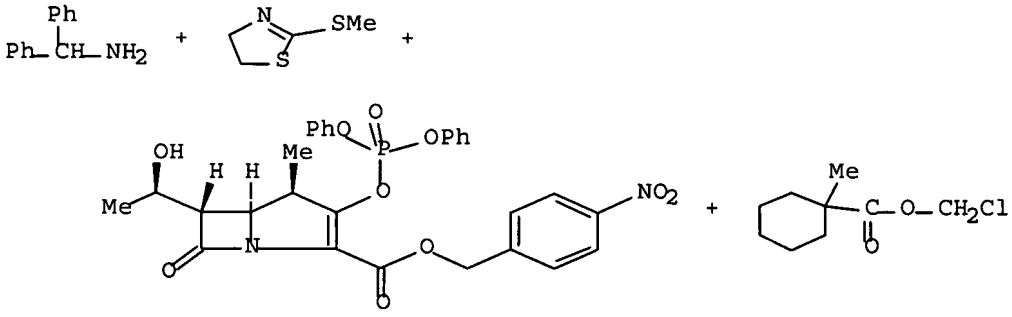
RX(118) OF 126 - 9 STEPS



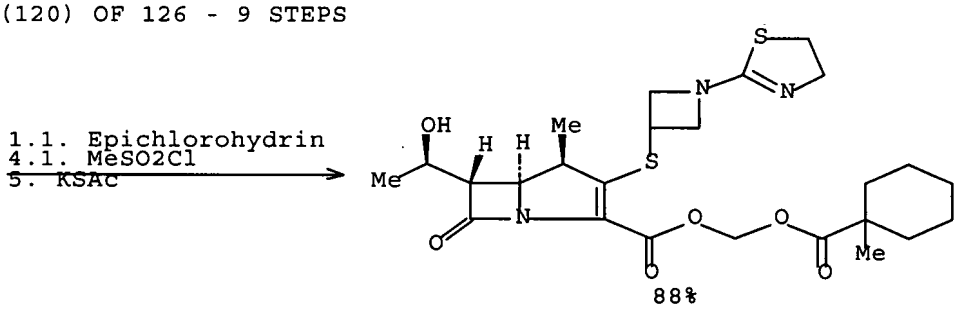
80%

CON: STEP(1.1) 1 day, room temperature
STEP(1.2) 3 days, 50 deg C
STEP(2.1) 4 hours, room temperature, 350 kPa
STEP(3.1) 23 hours, reflux; reflux -> 40 deg C
STEP(3.2) 2 hours, 40 deg C
STEP(4.1) 0.5 hours, 5 deg C
STEP(4.2) 10 minutes, room temperature
STEP(5) 5.5 hours, 100 deg C
STEP(6.1) 10 minutes, 5 deg C
STEP(6.2) 15 minutes
STEP(7.1) 2 hours, -20 deg C
STEP(7.2) 0.5 hours, 5 deg C
STEP(8.1) 1.5 hours, room temperature, 400 kPa
STEP(8.2) pH 5.6
STEP(9.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(9.2) 5 deg C, pH 4
STEP(9.3) pH 7.6

RX(120) OF 126 - 9 STEPS

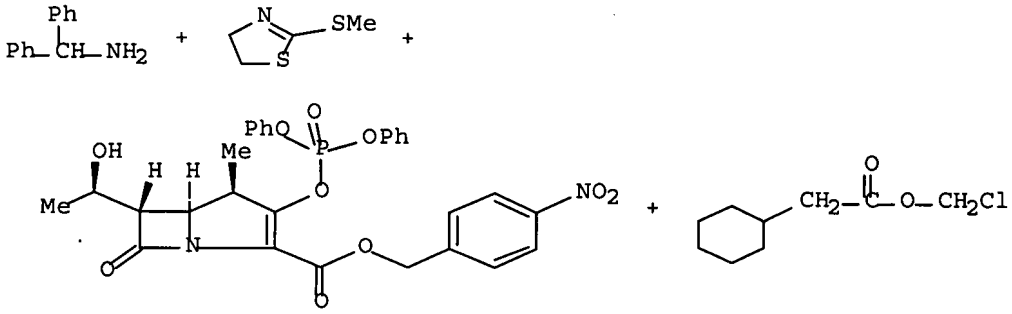


RX(120) OF 126 - 9 STEPS



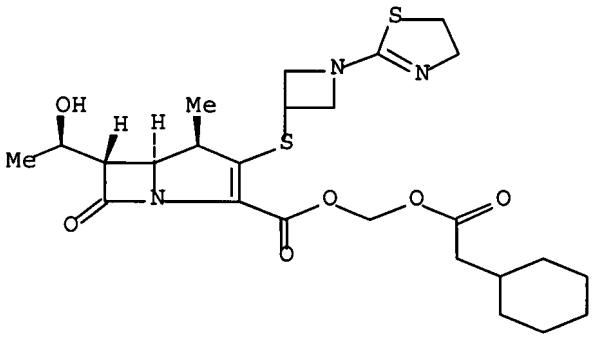
CON: STEP(1.1) 1 day, room temperature
STEP(1.2) 3 days, 50 deg C
STEP(2.1) 4 hours, room temperature, 350 kPa
STEP(3.1) 23 hours, reflux; reflux -> 40 deg C
STEP(3.2) 2 hours, 40 deg C
STEP(4.1) 0.5 hours, 5 deg C
STEP(4.2) 10 minutes, room temperature
STEP(5) 5.5 hours, 100 deg C
STEP(6.1) 10 minutes, 5 deg C
STEP(6.2) 15 minutes
STEP(7.1) 2 hours, -20 deg C
STEP(7.2) 0.5 hours, 5 deg C
STEP(8.1) 1.5 hours, room temperature, 400 kPa
STEP(8.2) pH 5.6
STEP(9.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(9.2) 5 deg C, pH 4
STEP(9.3) pH 7.6

RX(121) OF 126 - 9 STEPS



RX(121) OF 126 - 9 STEPS

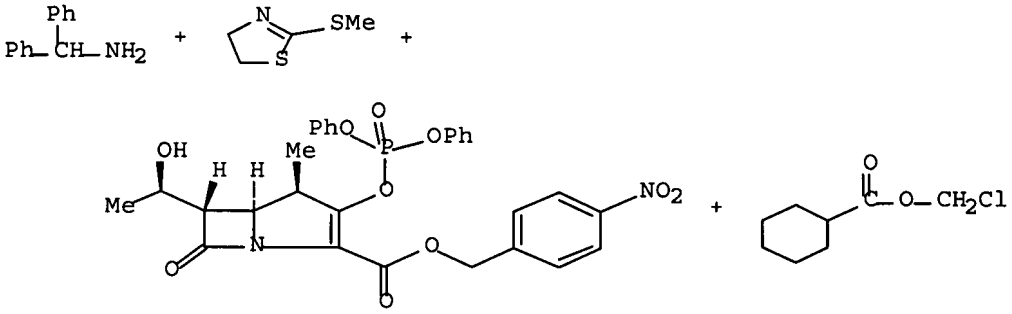
1.1. Epichlorohydrin
4.1. MeSO2Cl
5. KSAc



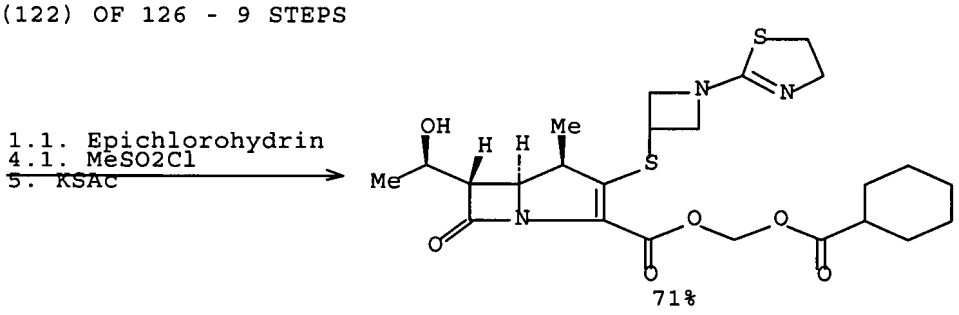
76%

CON: STEP(1.1) 1 day, room temperature
STEP(1.2) 3 days, 50 deg C
STEP(2.1) 4 hours, room temperature, 350 kPa
STEP(3.1) 23 hours, reflux; reflux -> 40 deg C
STEP(3.2) 2 hours, 40 deg C
STEP(4.1) 0.5 hours, 5 deg C
STEP(4.2) 10 minutes, room temperature
STEP(5) 5.5 hours, 100 deg C
STEP(6.1) 10 minutes, 5 deg C
STEP(6.2) 15 minutes
STEP(7.1) 2 hours, -20 deg C
STEP(7.2) 0.5 hours, 5 deg C
STEP(8.1) 1.5 hours, room temperature, 400 kPa
STEP(8.2) pH 5.6
STEP(9.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(9.2) 5 deg C, pH 4
STEP(9.3) pH 7.6

RX(122) OF 126 - 9 STEPS

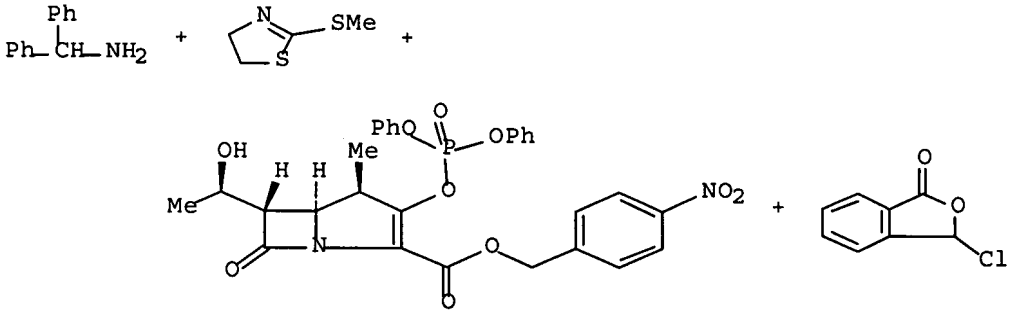


RX(122) OF 126 - 9 STEPS

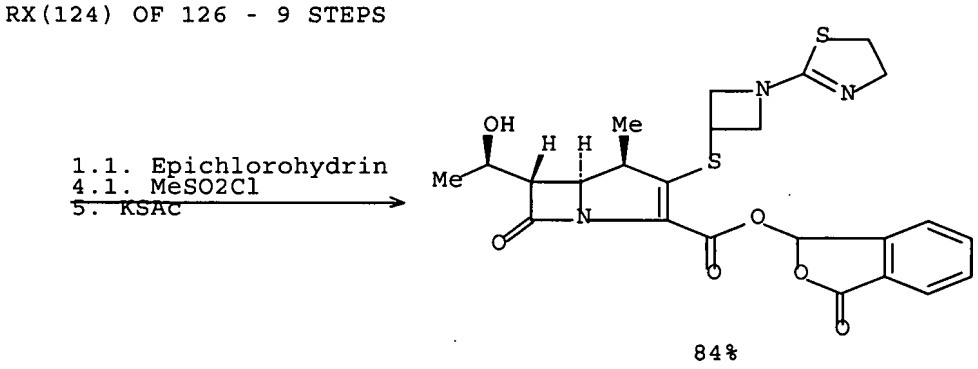


CON: STEP(1.1) 1 day, room temperature
STEP(1.2) 3 days, 50 deg C
STEP(2.1) 4 hours, room temperature, 350 kPa
STEP(3.1) 23 hours, reflux; reflux -> 40 deg C
STEP(3.2) 2 hours, 40 deg C
STEP(4.1) 0.5 hours, 5 deg C
STEP(4.2) 10 minutes, room temperature
STEP(5) 5.5 hours, 100 deg C
STEP(6.1) 10 minutes, 5 deg C
STEP(6.2) 15 minutes
STEP(7.1) 2 hours, -20 deg C
STEP(7.2) 0.5 hours, 5 deg C
STEP(8.1) 1.5 hours, room temperature, 400 kPa
STEP(8.2) pH 5.6
STEP(9.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(9.2) 5 deg C, pH 4
STEP(9.3) pH 7.6

RX(124) OF 126 - 9 STEPS



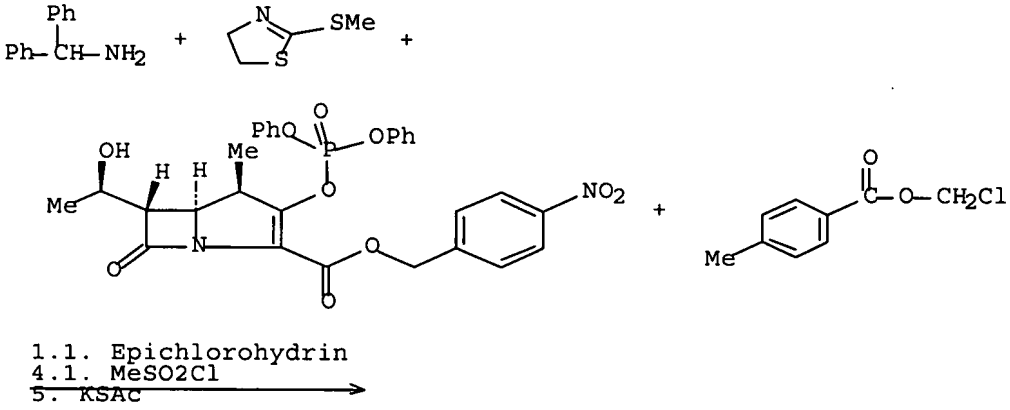
RX(124) OF 126 - 9 STEPS



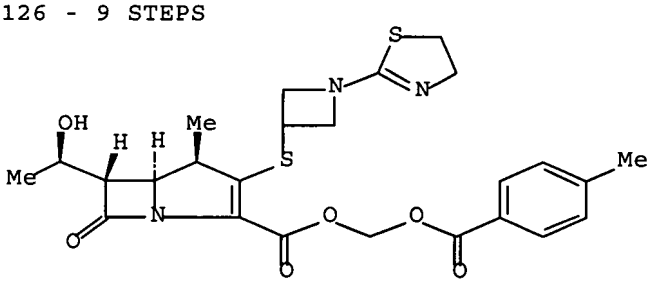
84%

CON: STEP(1.1) 1 day, room temperature
STEP(1.2) 3 days, 50 deg C
STEP(2.1) 4 hours, room temperature, 350 kPa
STEP(3.1) 23 hours, reflux; reflux -> 40 deg C
STEP(3.2) 2 hours, 40 deg C
STEP(4.1) 0.5 hours, 5 deg C
STEP(4.2) 10 minutes, room temperature
STEP(5) 5.5 hours, 100 deg C
STEP(6.1) 10 minutes, 5 deg C
STEP(6.2) 15 minutes
STEP(7.1) 2 hours, -20 deg C
STEP(7.2) 0.5 hours, 5 deg C
STEP(8.1) 1.5 hours, room temperature, 400 kPa
STEP(8.2) pH 5.6
STEP(9.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(9.2) 5 deg C, pH 4
STEP(9.3) pH 7.6

RX(125) OF 126 - 9 STEPS



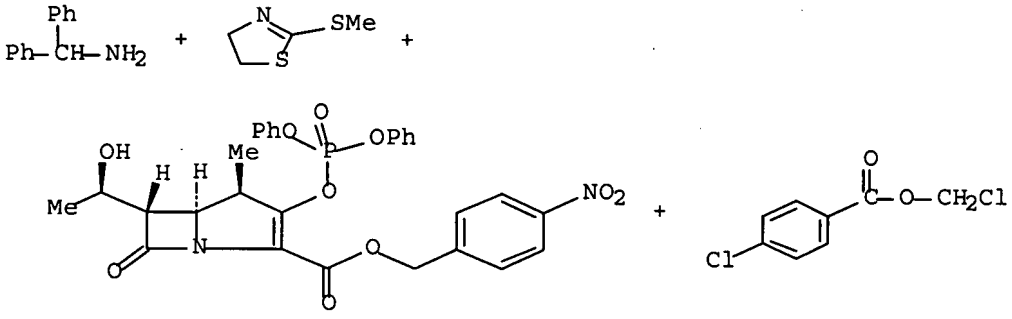
RX(125) OF 126 - 9 STEPS



84%

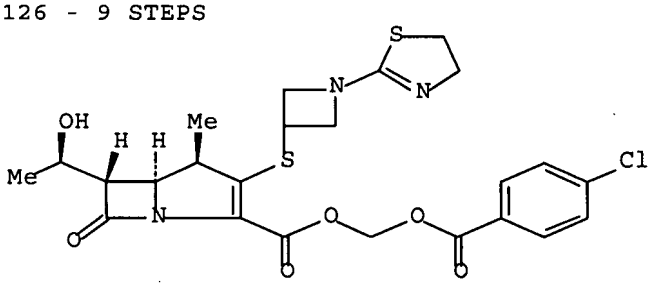
CON: STEP(1.1) 1 day, room temperature
STEP(1.2) 3 days, 50 deg C
STEP(2.1) 4 hours, room temperature, 350 kPa
STEP(3.1) 23 hours, reflux; reflux -> 40 deg C
STEP(3.2) 2 hours, 40 deg C
STEP(4.1) 0.5 hours, 5 deg C
STEP(4.2) 10 minutes, room temperature
STEP(5) 5.5 hours, 100 deg C
STEP(6.1) 10 minutes, 5 deg C
STEP(6.2) 15 minutes
STEP(7.1) 2 hours, -20 deg C
STEP(7.2) 0.5 hours, 5 deg C
STEP(8.1) 1.5 hours, room temperature, 400 kPa
STEP(8.2) pH 5.6
STEP(9.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(9.2) 5 deg C, pH 4
STEP(9.3) pH 7.6

RX(126) OF 126 - 9 STEPS



1.1. Epichlorohydrin
4.1. MeSO2Cl
5. KSAc

RX(126) OF 126 - 9 STEPS



81%

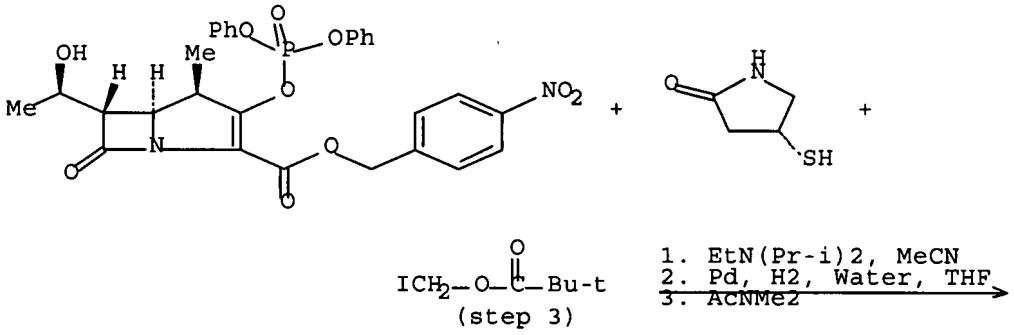
CON: STEP(1.1) 1 day, room temperature
STEP(1.2) 3 days, 50 deg C
STEP(2.1) 4 hours, room temperature, 350 kPa
STEP(3.1) 23 hours, reflux; reflux -> 40 deg C
STEP(3.2) 2 hours, 40 deg C
STEP(4.1) 0.5 hours, 5 deg C
STEP(4.2) 10 minutes, room temperature
STEP(5) 5.5 hours, 100 deg C
STEP(6.1) 10 minutes, 5 deg C
STEP(6.2) 15 minutes
STEP(7.1) 2 hours, -20 deg C
STEP(7.2) 0.5 hours, 5 deg C
STEP(8.1) 1.5 hours, room temperature, 400 kPa
STEP(8.2) pH 5.6
STEP(9.1) 4 hours, 45 deg C; 45 deg C -> 5 deg C
STEP(9.2) 5 deg C, pH 4
STEP(9.3) pH 7.6

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 4 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 127:156255 CASREACT Full-text
TITLE: Synthesis and structure-activity relationships of a novel oral carbapenem, CS-834
AUTHOR(S): Miyauchi, Masao; Endo, Rokuro; Hisaoka, Masafumi; Yasuda, Hiroshi; Kawamoto, Isao
CORPORATE SOURCE: Research Laboratories, Sankyo Co., Ltd., Shinagawaku, 140, Japan
SOURCE: Journal of Antibiotics (1997), 50(5), 429-439
CODEN: JANTAJ; ISSN: 0021-8820
PUBLISHER: Japan Antibiotics Research Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have studied an ester prodrug of a carbapenem to develop a potent orally active β-lactam antibiotic. A variety of 1β-methylcarbapenem derivs. have been synthesized. The authors have found that some derivs. having an amide group in the C-2 side chain show potent and well balanced antibacterial activities as well as high stability against dehydropeptidase-I. Oral absorption of derivs. has been optimized by modifying the C-3 ester promoiety. Pivaloyloxymethyl (1R,5S,6S)-6[(R)-1-hydroxyethyl]-1-methyl-2-[(R)-5-oxopyrrolidin-3-ylthio]- 1-carbapen-2-em-3-carboxylate, CS-834, has been selected as the most promising compound for further evaluation.

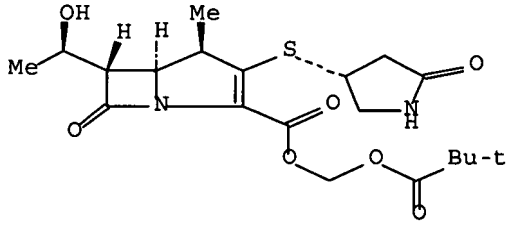
RX(27) OF 63 - 3 STEPS



(step 3)

1. EtN(Pr-i)2, MeCN
2. Pd, H2, Water, THF
3. AcNMe2

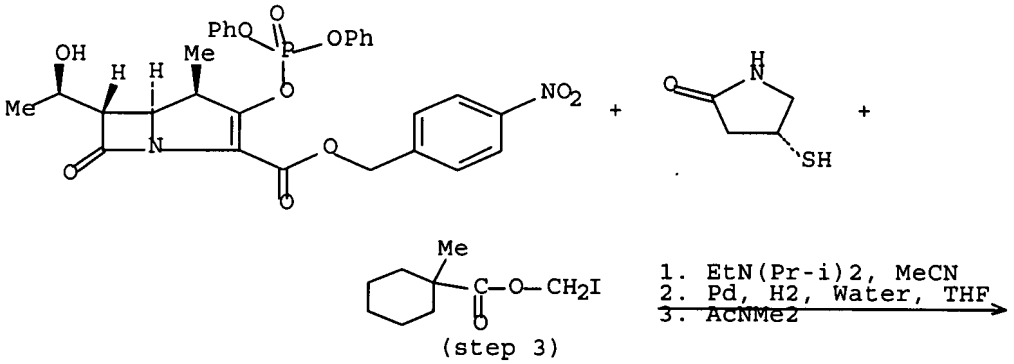
RX(27) OF 63 - 3 STEPS



61%

NOTE: 2) PHOSPHATE BUFFER, S-ANALOG SIMILARLY PREPD.

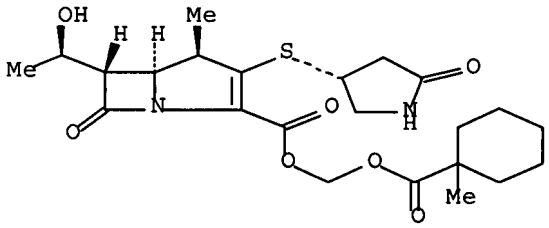
RX(28) OF 63 - 3 STEPS



(step 3)

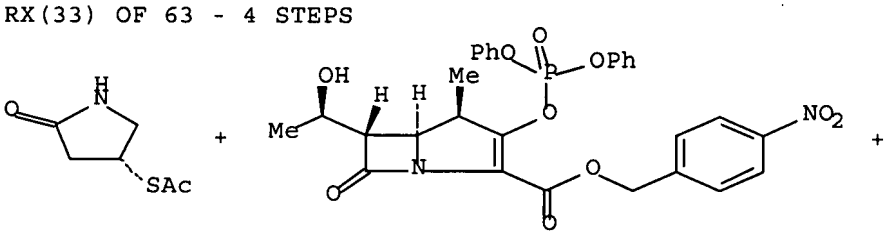
1. EtN(Pr-i)2, MeCN
2. Pd, H2, Water, THF
3. AcNMe2

RX(28) OF 63 - 3 STEPS

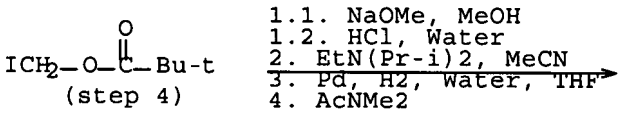


NOTE: 2) PHOSPHATE BUFFER, S-ANALOG SIMILARLY PREPD.

RX(33) OF 63 - 4 STEPS



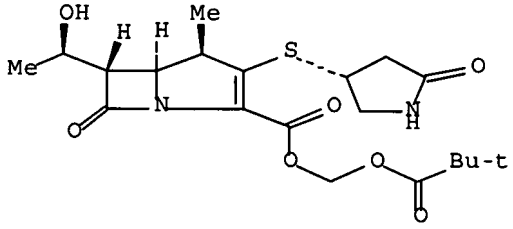
(step 2)



(step 4)

1.1. NaOMe, MeOH
1.2. HCl, Water
2. EtN(Pr-i)2, MeCN
3. Pd, H2, Water, THF
4. AcNMe2

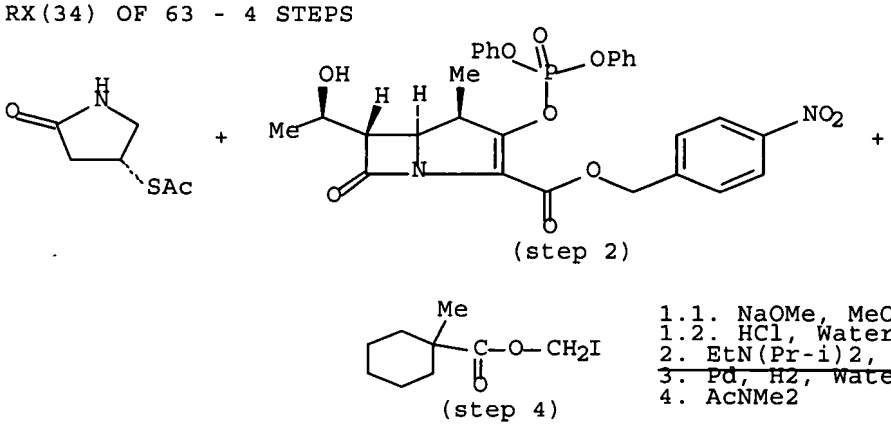
RX(33) OF 63 - 4 STEPS



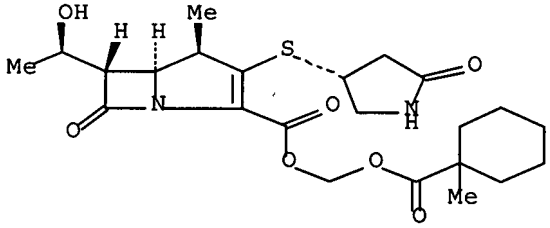
61%

NOTE: 1) S-ANALOG SIMILARLY PREPD., 3) PHOSPHATE BUFFER, S-ANALOG SIMILARLY PREPD.

RX(34) OF 63 - 4 STEPS

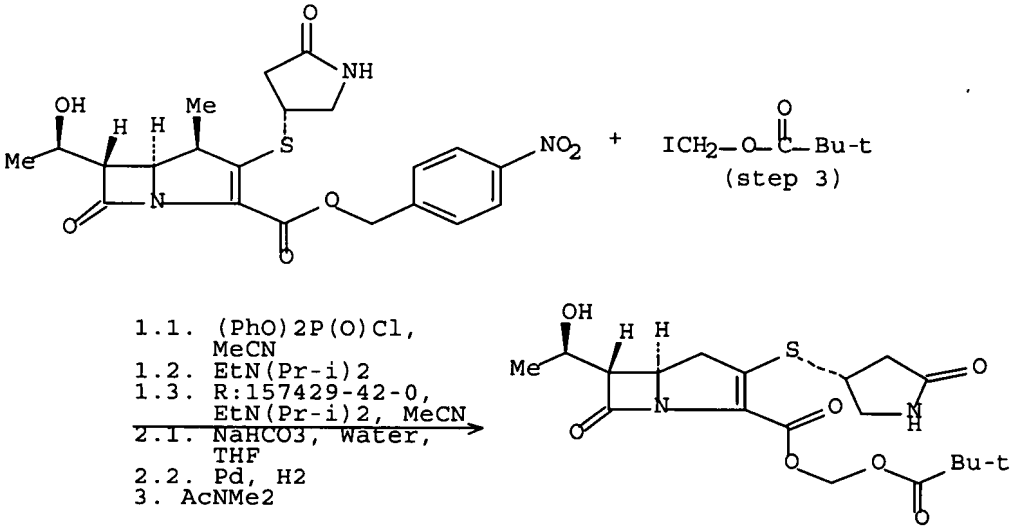


RX(34) OF 63 - 4 STEPS

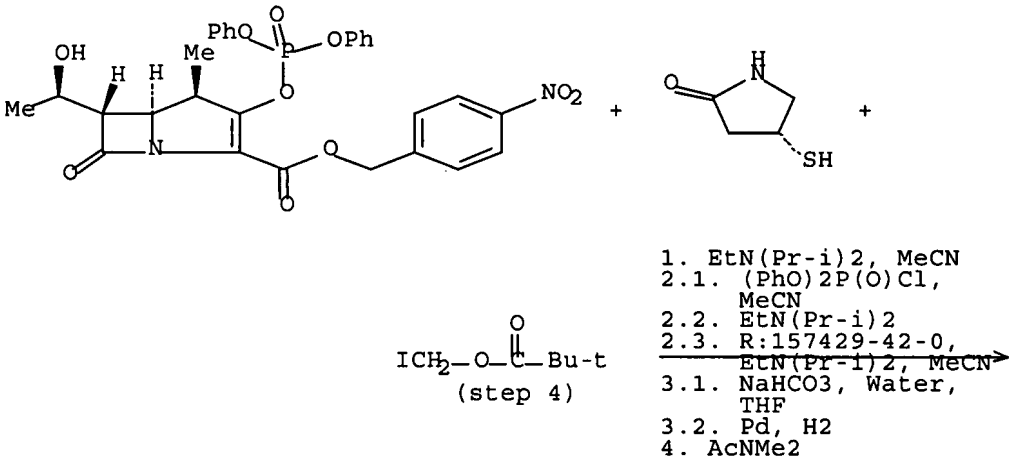


NOTE: 1) S-ANALOG SIMILARLY PREPD., 3) PHOSPHATE BUFFER, S-ANALOG SIMILARLY PREPD.

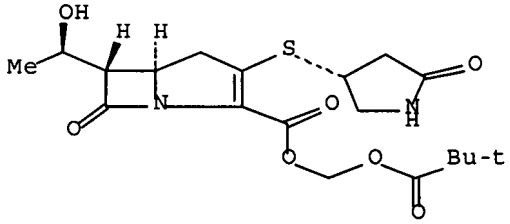
RX(45) OF 63 - 3 STEPS



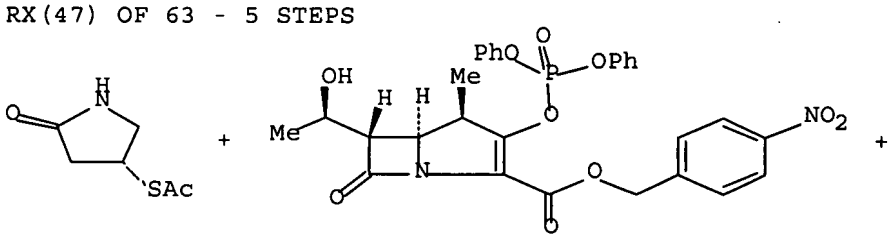
RX(46) OF 63 - 4 STEPS

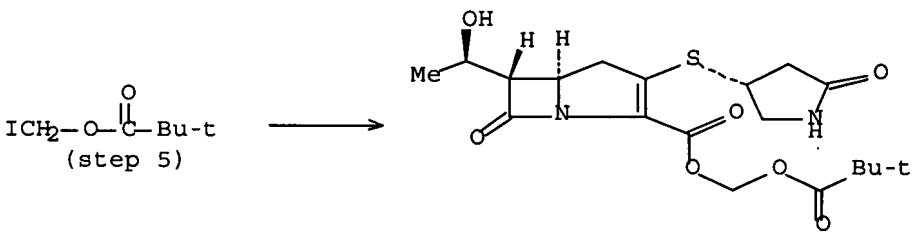


RX(46) OF 63 - 4 STEPS



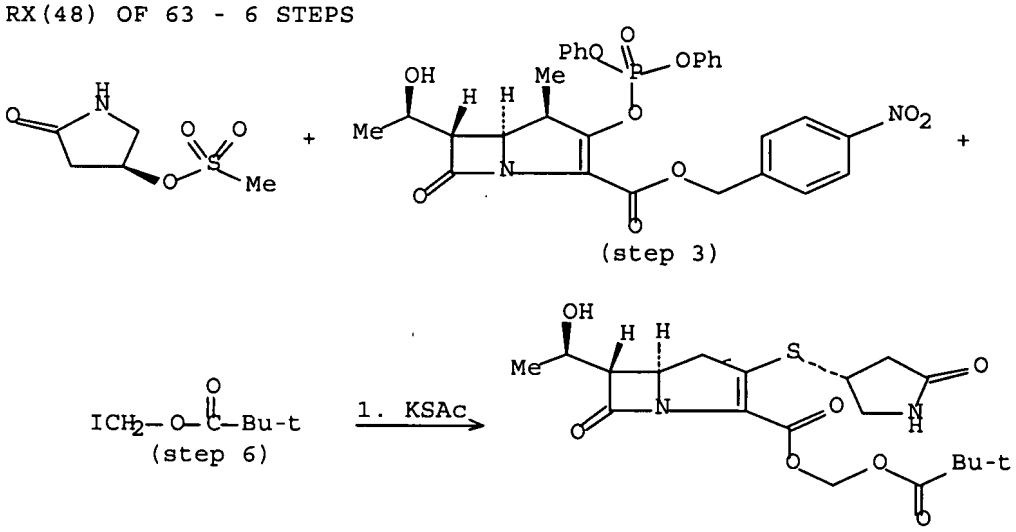
RX(47) OF 63 - 5 STEPS





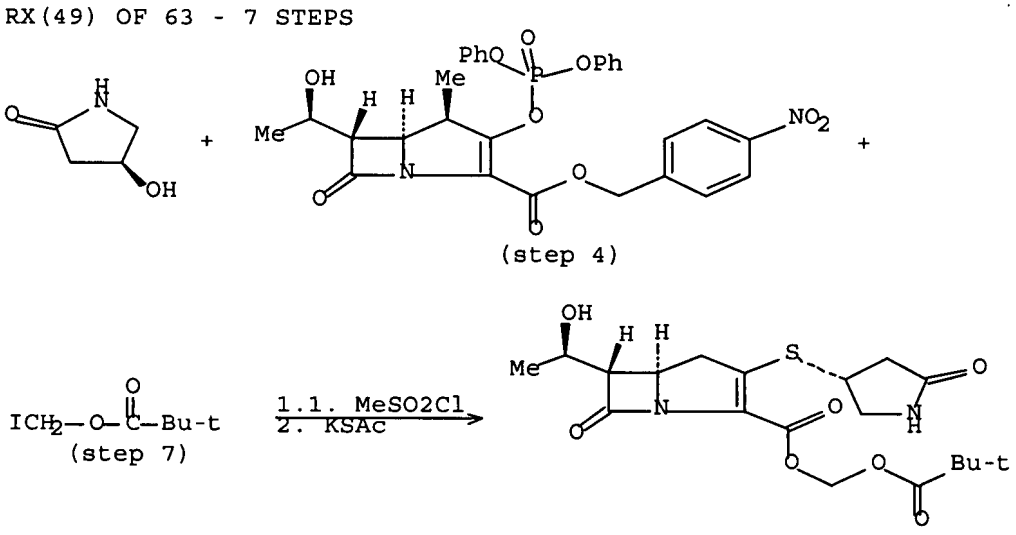
NOTE: 1) S-ANALOG SIMILARLY PREPD.

RX(48) OF 63 - 6 STEPS



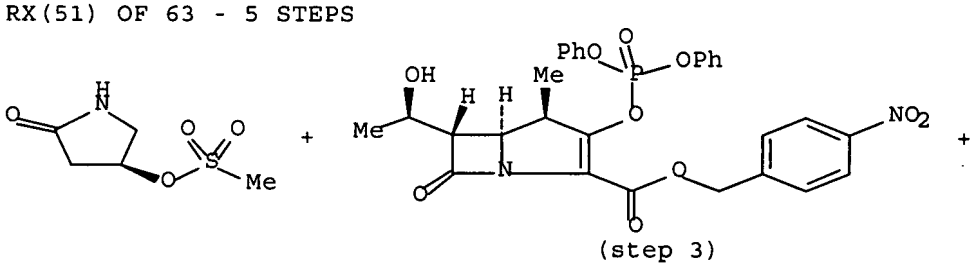
NOTE: 2) S-ANALOG SIMILARLY PREPD.

RX(49) OF 63 - 7 STEPS

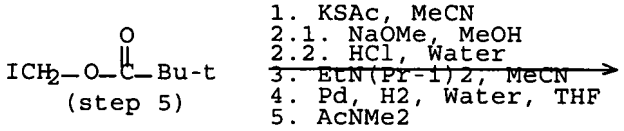


NOTE: 3) S-ANALOG SIMILARLY PREPD.

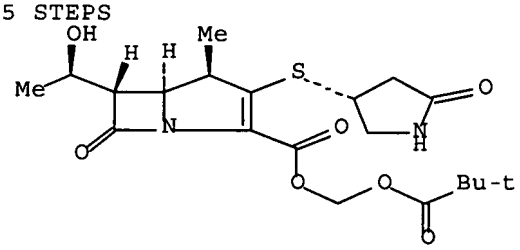
RX(51) OF 63 - 5 STEPS



(step 3)



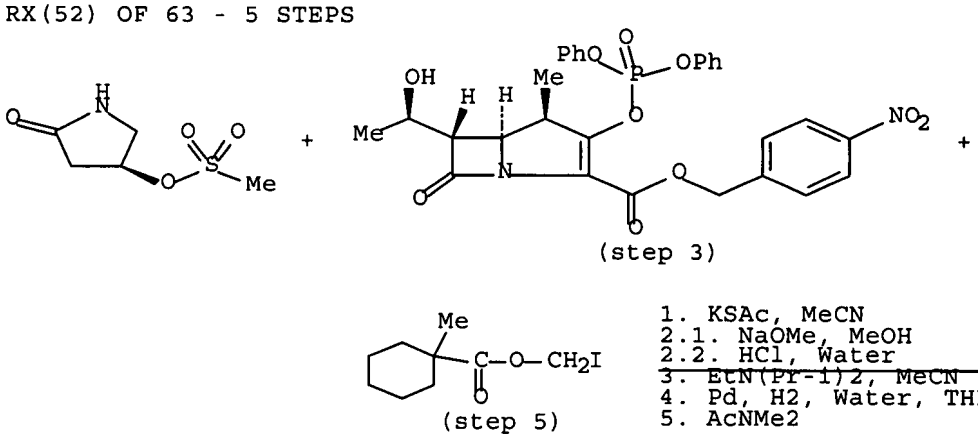
RX(51) OF 63 - 5 STEPS



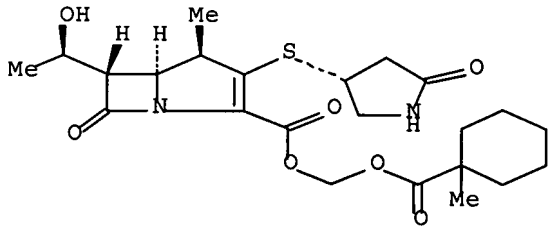
61%

NOTE: 2) S-ANALOG SIMILARLY PREPD., 4) PHOSPHATE BUFFER, S-ANALOG SIMILARLY PREPD.

RX(52) OF 63 - 5 STEPS

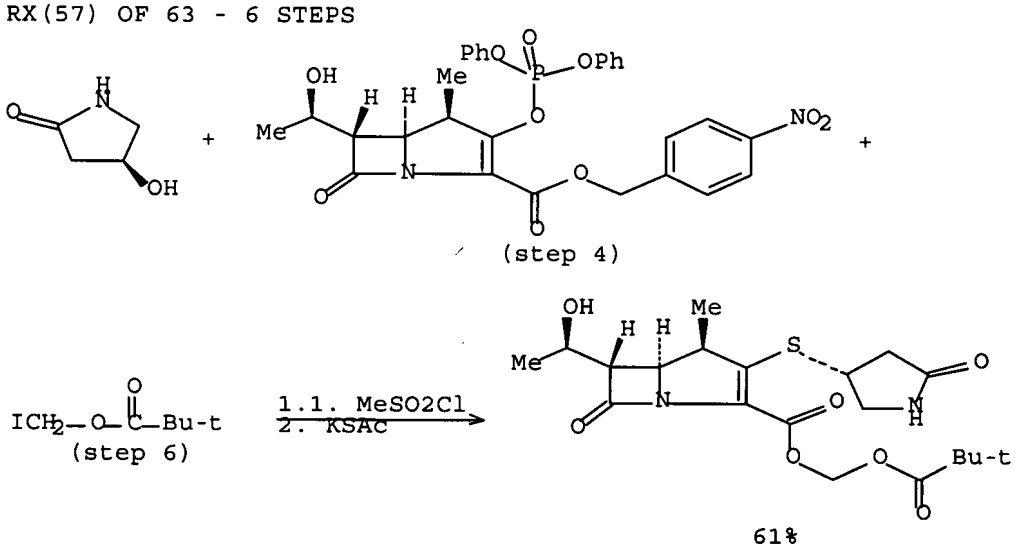


RX(52) OF 63 - 5 STEPS



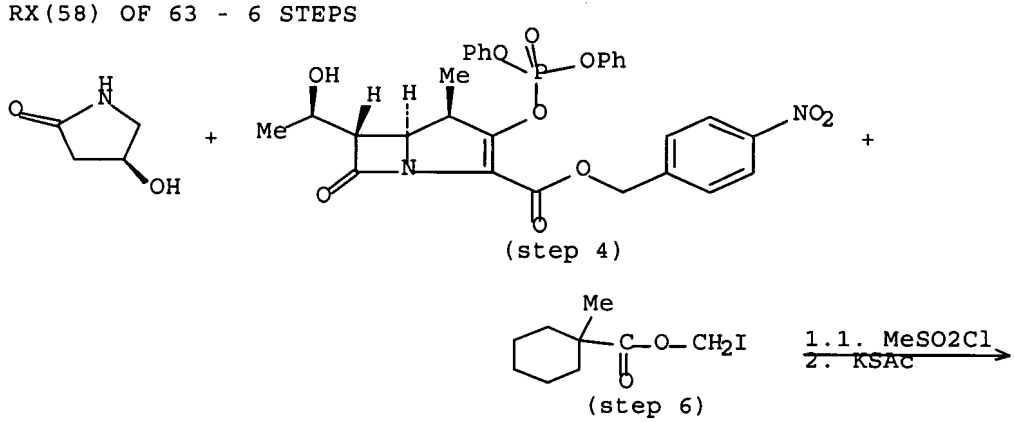
NOTE: 2) S-ANALOG SIMILARLY PREPD., 4) PHOSPHATE BUFFER, S-ANALOG SIMILARLY PREPD.

RX(57) OF 63 - 6 STEPS



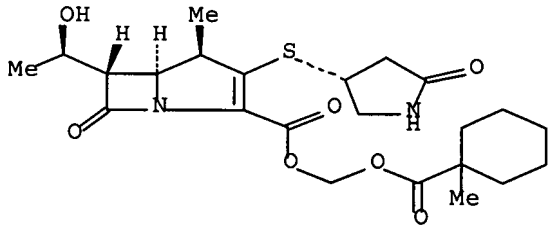
NOTE: 3) S-ANALOG SIMILARLY PREPD., 5) PHOSPHATE BUFFER, S-ANALOG SIMILARLY PREPD.

RX(58) OF 63 - 6 STEPS



1

RX(58) OF 63 - 6 STEPS



NOTE: 3) S-ANALOG SIMILARLY PREPD., 5) PHOSPHATE BUFFER, S-ANALOG SIMILARLY PREPD.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 4 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 125:328328 CASREACT Full-text

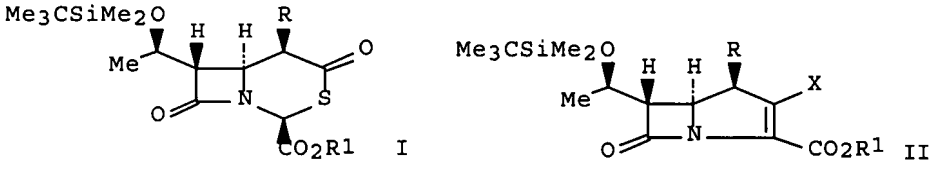
TITLE: A New Synthesis of 1β-Alkylcarbapenems Utilizing Eschenmoser Sulfide Contraction of the Novel Thiazinone Intermediates

AUTHOR(S): Sakurai, Osamu; Ogiku, Tsuyoshi; Takahashi, Masami; Hayashi, Masahito; Yamanaka, Takeshi; Horikawa, Hiroshi; Iwasaki, Tameo

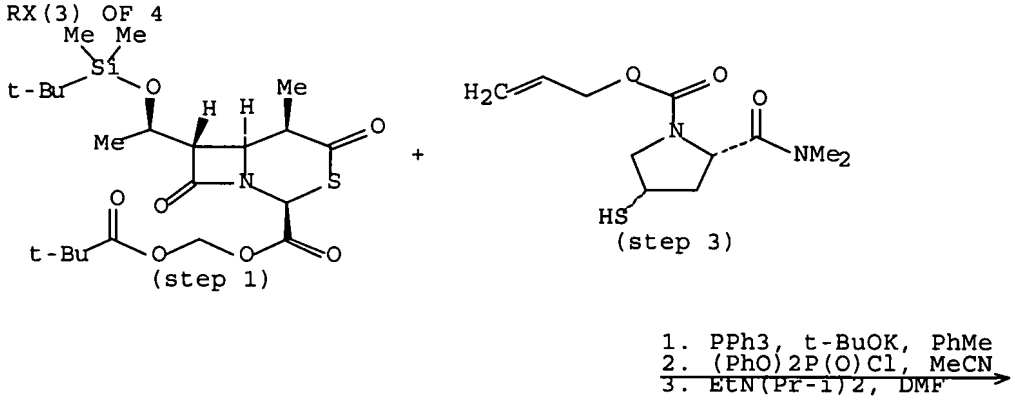
CORPORATE SOURCE: Lead Generation Research Laboratory, Tanabe Seiyaku Co. Ltd., Yodogawa, 532, Japan

SOURCE: Journal of Organic Chemistry (1996), 61(22), 7889-7894

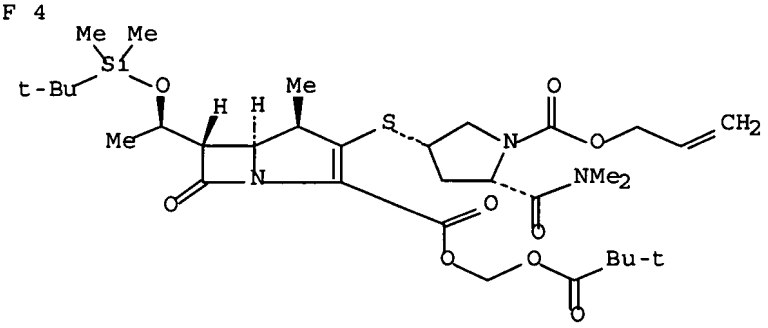
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB Novel syntheses of the 1β-alkylcarbapenems were achieved on the basis of Eschenmoser sulfide contraction of new bicyclic 1,3-thiazinone intermediates. 1,3-Thiazinones I [R = Me, CH2CH2OSiMe2CMe3; R1 = allyl, CH2O2CCMe3] were effectively prepared from thioesters using a C(4)-S bond formation process. The sulfide contraction reactions were performed by treatment of I with base (NaH or KOCMe3) in the presence of triphenylphosphine to generate the carbapenem enolates which were trapped by (PhO)2POCl followed by reaction with mercaptans to afford carbapenems II [X = SCH2CH2NHCO2CH2CH:CH2, (3S,5S)-1-allyloxycarbonyl-2-N,N- dimethylcarbamoyl-5-pyrrolidinylthio].



RX(3) OF 4

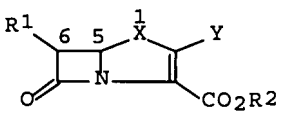


39%

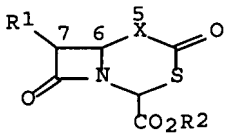
L8 ANSWER 4 OF 4 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 120:217089 CASREACT Full-text
TITLE: Process for preparing beta-lactam derivatives (carbapenems) and azathiabicycloalkanes as synthetic intermediates thereof
INVENTOR(S): Horikawa, Hiroshi; Kondo, Kazuhiko; Iwasaki, Tameo
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 559533	A1	19930908	EP 1993-400506	19930226
EP 559533	B1	19980722		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 05279367	A	19931026	JP 1992-99023	19920306
JP 2569455	B2	19970108		
CA 2085540	A1	19930907	CA 1993-2085540	19930217
US 5414081	A	19950509	US 1993-18407	19930217
AT 168693	T	19980815	AT 1993-400506	19930226
ES 2119872	T3	19981016	ES 1993-400506	19930226
US 5589592	A	19961231	US 1995-393395	19950407
PRIORITY APPLN. INFO.:			JP 1992-99023	19920306
			US 1993-18407	19930217

OTHER SOURCE(S): MARPAT 120:217089
GI



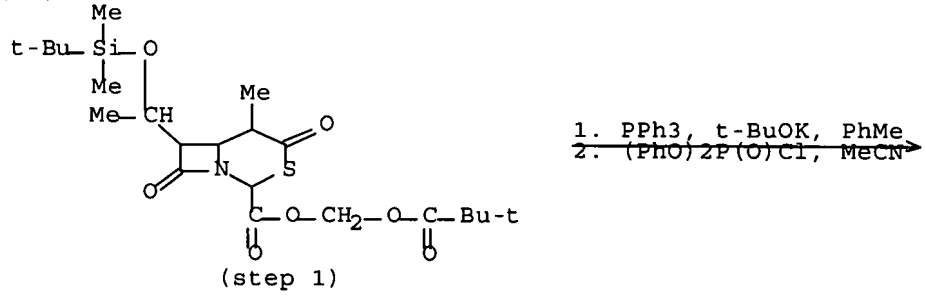
I



II

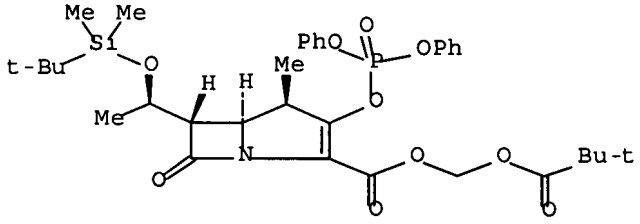
AB β-Lactams I [R1 = (un)protected hydroxyalkyl or amino; R2 = H, ester residue; X = CH2, alkylidene, S, ACH2; A = S, O, CH2; Y = OW, SR4; W = residue of active ester; R4 = organic group] and salts are prepared by treating 1-aza-3-thiabicycloalkanes II with a base and a desulfurizing agent, followed by reaction with an active esterifying agent and possibly with a mercaptan R4SH. Thus, (3S,4S)-3-[(R)-1-tert-butyldimethylsilyloxyethyl]-4- [(1R)-1-[2,2-bis(ethoxycarbonyl)ethylthiocarbonyl]ethyl]-1-[1-hydroxy-1-(pivaloyloxymethyloxycarbonyl)methyl]-2-azetidinone (preparation given) was treated with SOCl2 and pyridine in THF at -40 to -50° and the resultant 1-[1-chloro-1-(pivaloyloxymethyloxycarbonyl)methyl] derivative was cyclized by Et3N in DMF at -20 to 0° to give (5R,6S,7R)-II [R1 = (R)-Me3CSiMe2OCHMe, R2 = CH2OCOCMe3, X = β-CHMe]. Desulfurization of this with KOCMe3 and PPh3 in PhMe at -40 to -20° and esterification by quenching in a solution of ClP(O)(OPh)2 in MeCN gave (1R,5S,6S)-I [R1 = (R)-Me3CSiMe2OCHMe, R2 = CH2OCOCMe3, X = β-CHMe] [III; Y = OP(O)(OPh)2]. Treatment of this with (4S)-4-mercaptopyrrolidine-2-thione and (iso-Pr)2NEt in MeCN gave III [Y = (4R)-pyrrolidin-2-thion-4-ylthio]. A subset of I [i.e., R1 = MeCH(OR6); R2 as given; X = CHMe; Y = 1-R5-2-thioxopyrrolidinylthio; R5 = H, alkyl, alkoxyalkyl, dialkylaminoalkyl; R6 = H, protective group] are novel and show better antibacterial activity, stability to dehydropeptidase 1, oral absorbability, and toxicity in comparison to known analogs where Y is a 2-oxopyrrolidin-4-ylthio group.

RX(11) OF 52



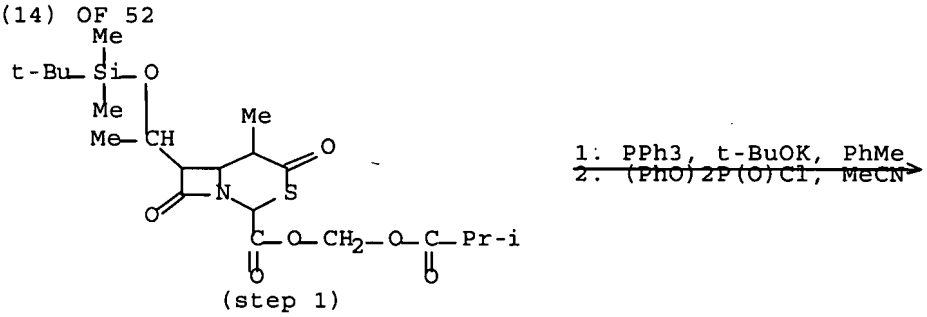
(step 1)

RX(11) OF 52



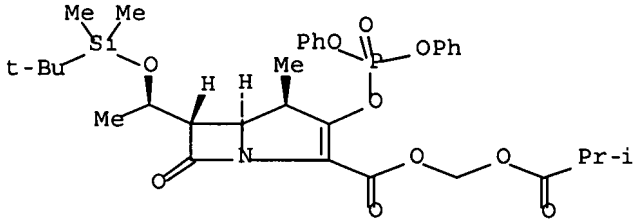
NOTE: -40 to -20.degree., then to 0.degree.

RX(14) OF 52



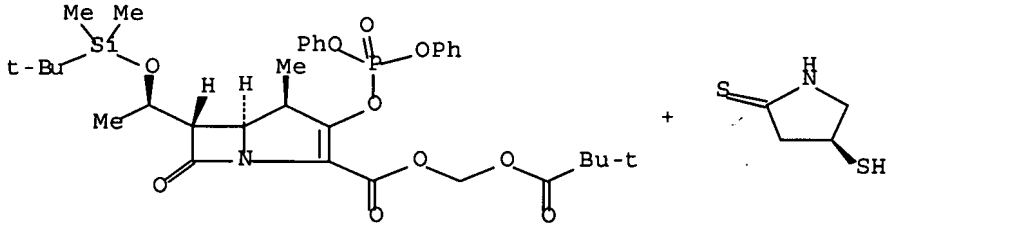
(step 1)

RX(14) OF 52

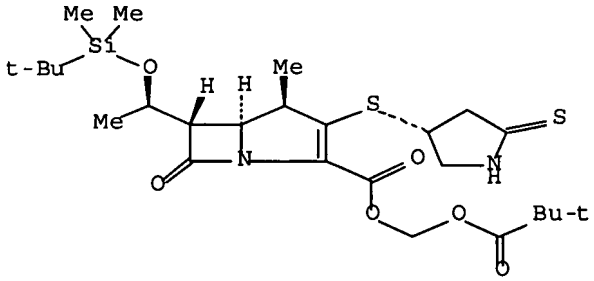


NOTE: -40 to -20.degree., then to 0.degree.

RX(16) OF 52

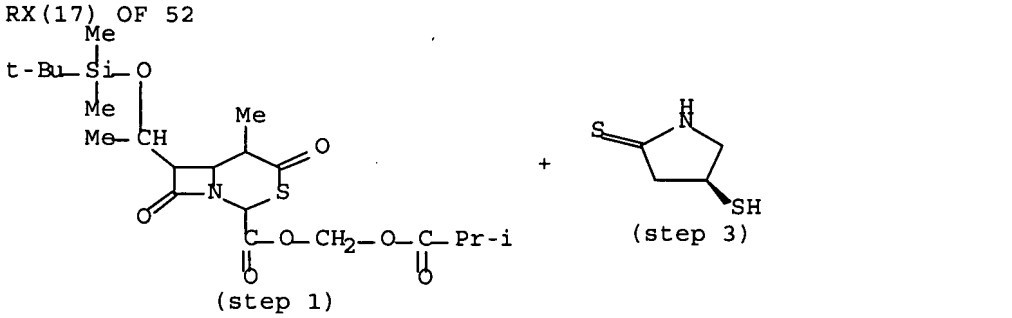


RX(16) OF 52

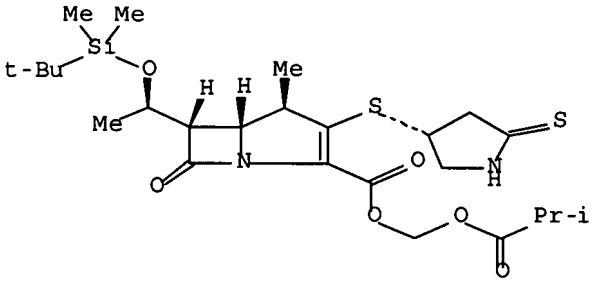


NOTE: -20 to 0.degree.

RX(17) OF 52

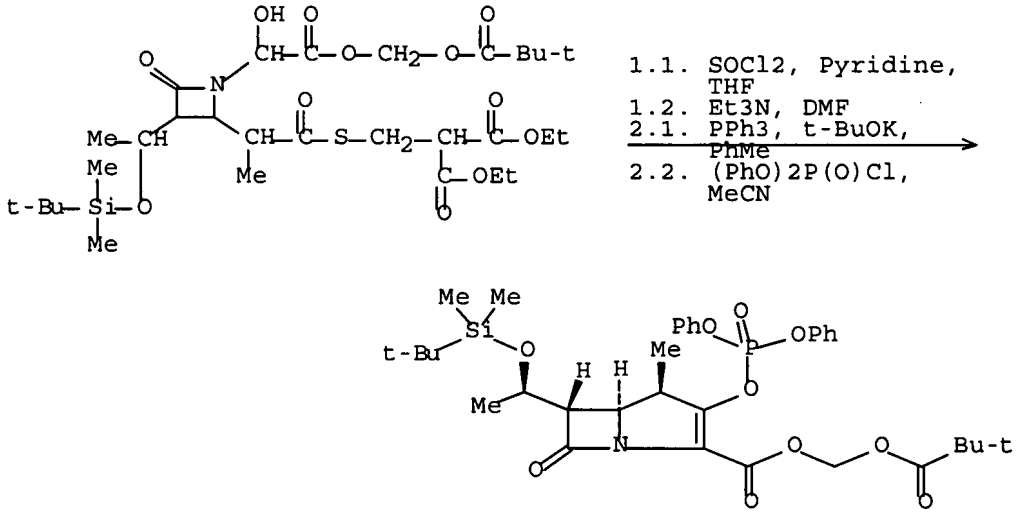


RX(17) OF 52



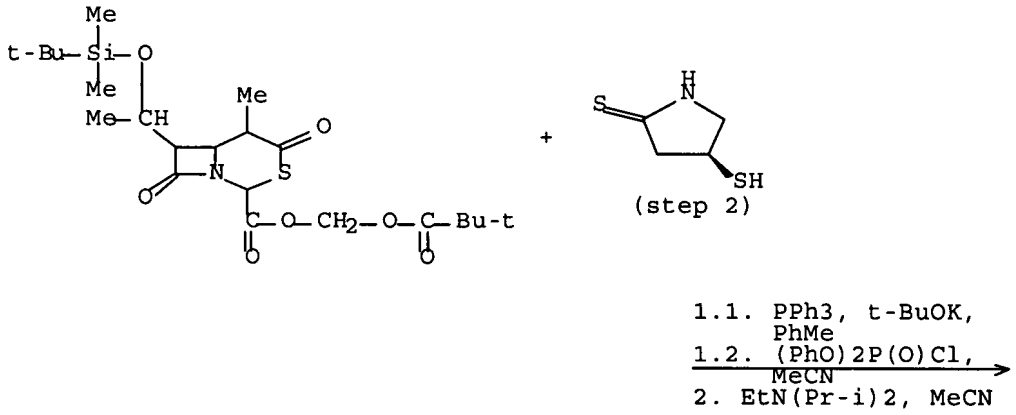
NOTE: -40.degree., then -40.degree., then -20 to -5.degree.

RX(27) OF 52 - 2 STEPS

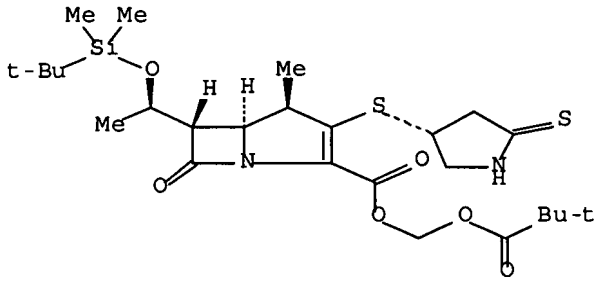


NOTE: 1) -50 to -40.degree., then -20 to 0.degree., 2) -40 to -20.degree., then to 0.degree.

RX(28) OF 52 - 2 STEPS

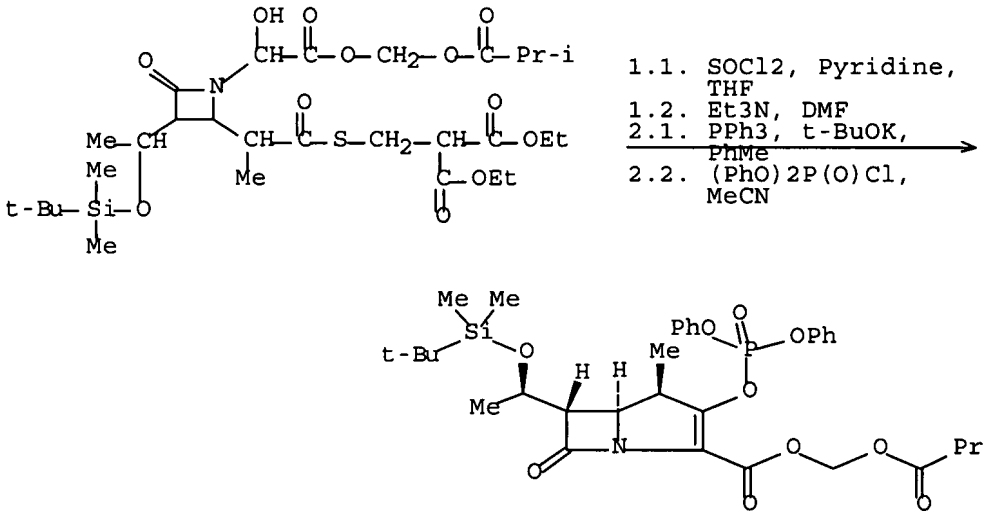


RX(28) OF 52 - 2 STEPS



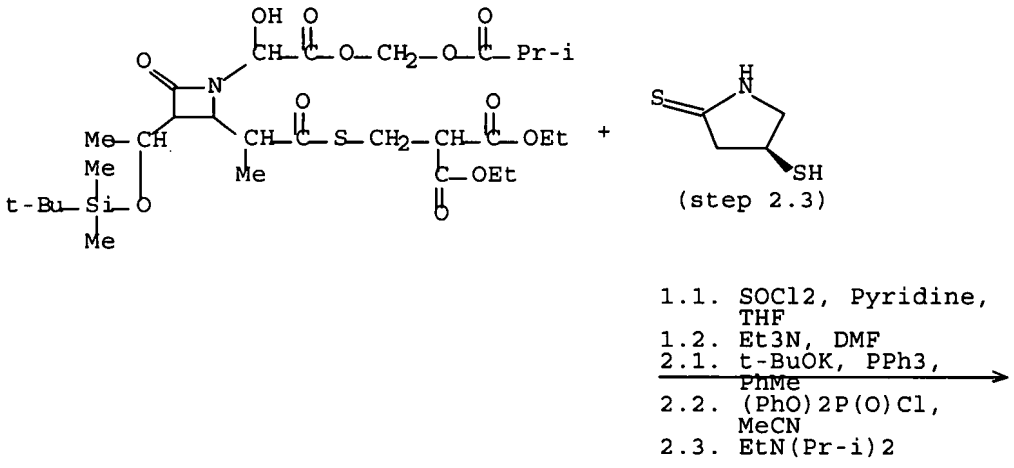
NOTE: 1) -40 to -20.degree., then to 0.degree., 2) -20 to 0.degree.

RX(30) OF 52 - 2 STEPS

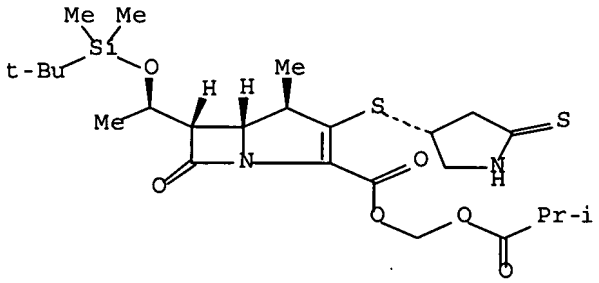


NOTE: 1) -50 to -40.degree., then -20 to 0.degree., 2) -40 to -20.degree., then to 0.degree.

RX(31) OF 52 - 2 STEPS

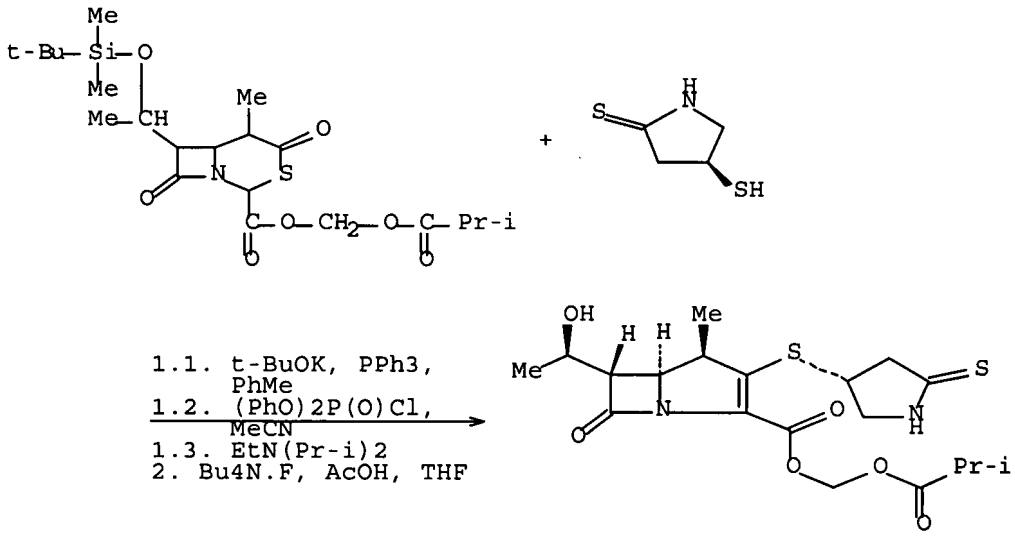


RX(31) OF 52 - 2 STEPS



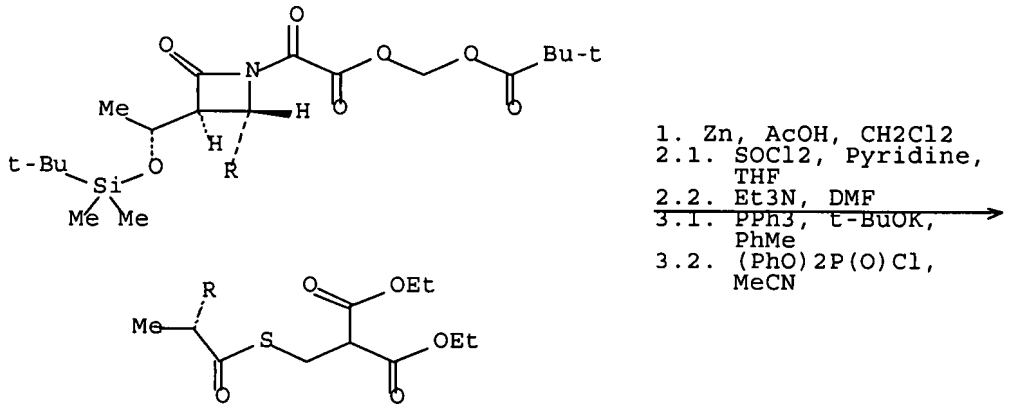
NOTE: 1) -50 to -40.degree., then -20 to 0.degree., 2) -40.degree., then -40.degree., then -20 to -5.degree.

RX(32) OF 52 - 2 STEPS

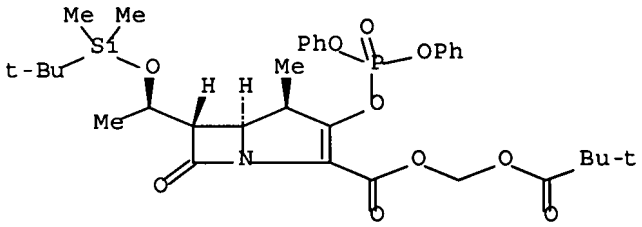


NOTE: 1) -40.degree., then -40.degree., then -20 to -5.degree., 2) room temp.

RX(41) OF 52 - 3 STEPS

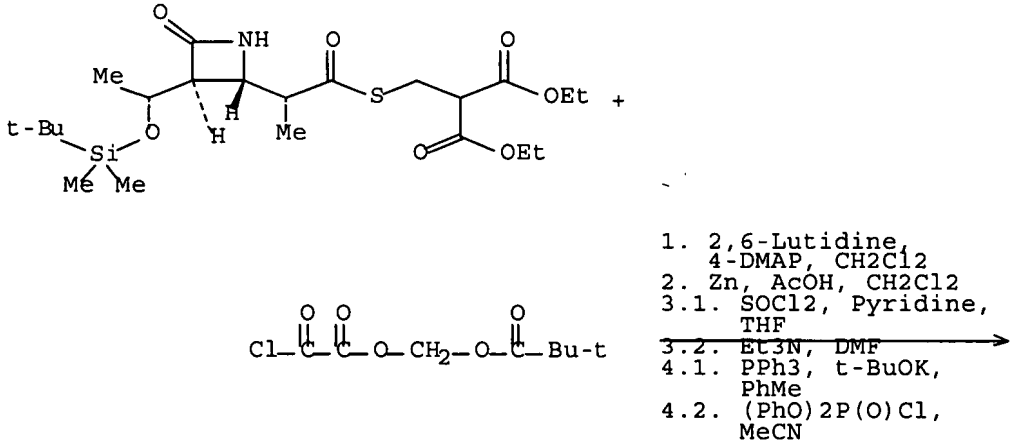


RX(41) OF 52 - 3 STEPS

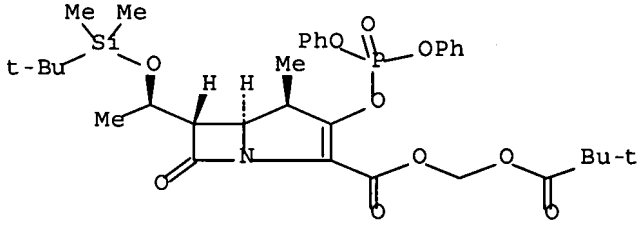


NOTE: 1) 0.degree., 2) -50 to -40.degree., then -20 to 0.degree., 3) -40 to -20.degree., then to 0.degree.

RX(42) OF 52 - 4 STEPS

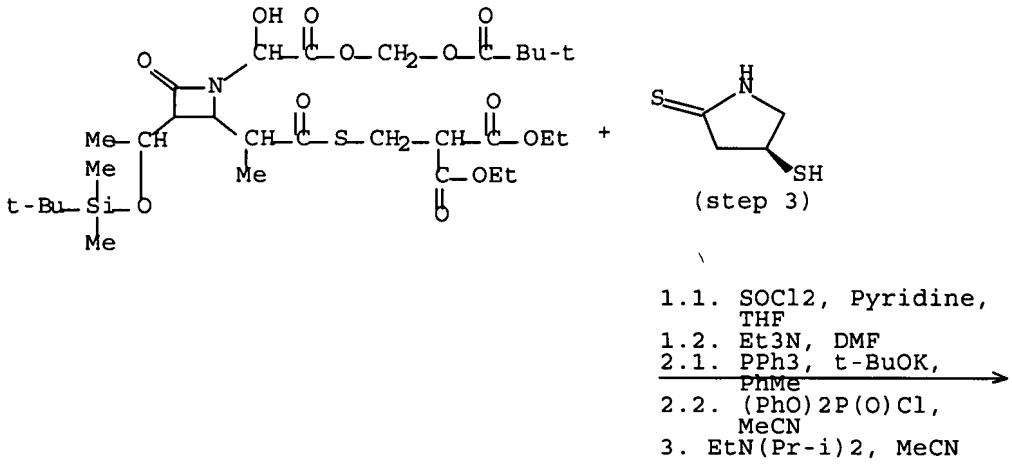


RX(42) OF 52 - 4 STEPS

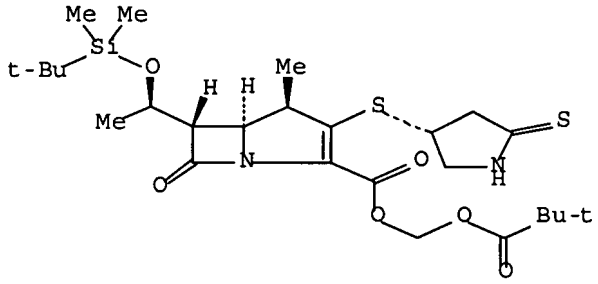


NOTE: 1) 0.degree., 2) 0.degree., 3) -50 to -40.degree., then -20 to 0.degree., 4) -40 to -20.degree., then to 0.degree.

RX(43) OF 52 - 3 STEPS

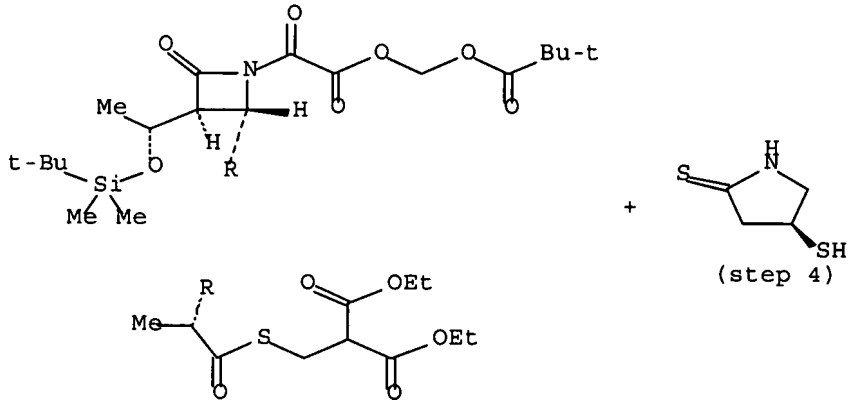


RX(43) OF 52 - 3 STEPS

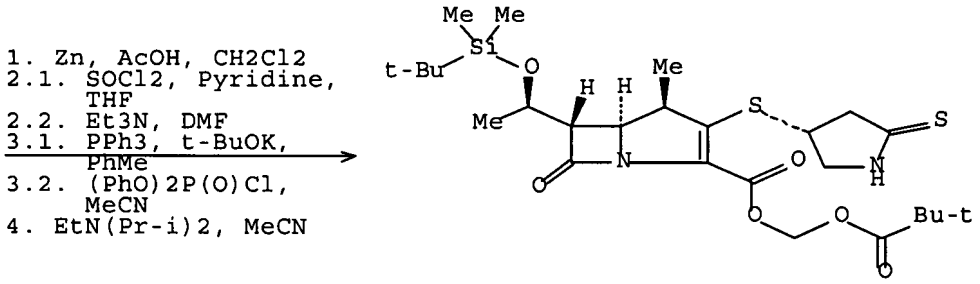


NOTE: 1) -50 to -40.degree., then -20 to 0.degree., 2) -40 to -20.degree., then to 0.degree., 3) -20 to 0.degree.

RX(44) OF 52 - 4 STEPS

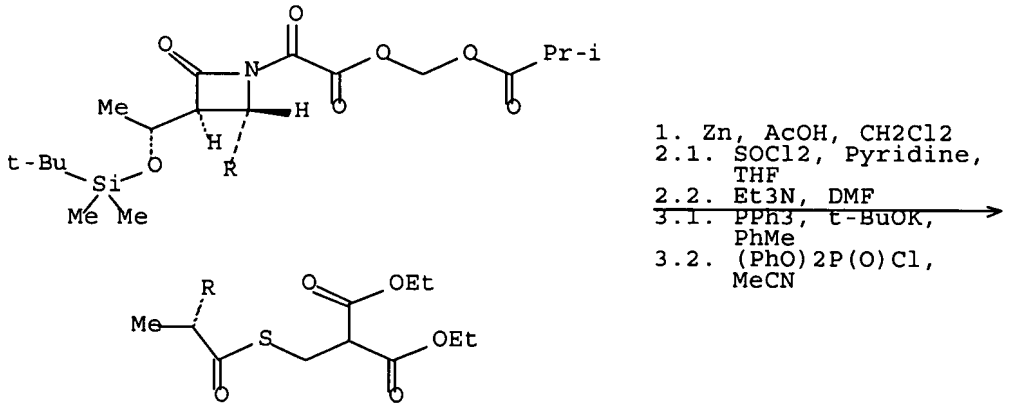


RX(44) OF 52 - 4 STEPS

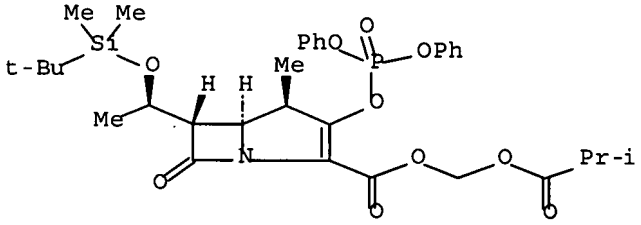


NOTE: 1) 0.degree., 2) -50 to -40.degree., then -20 to 0.degree., 3) -40 to -20.degree., then to 0.degree., 4) -20 to 0.degree.

RX(45) OF 52 - 3 STEPS

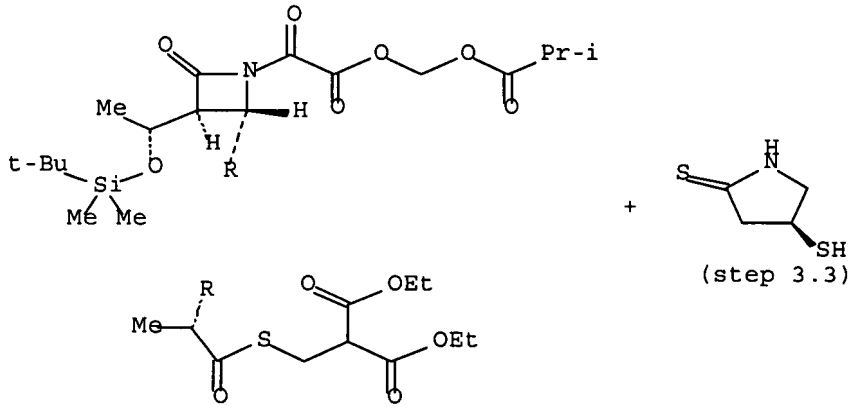


RX(45) OF 52 - 3 STEPS

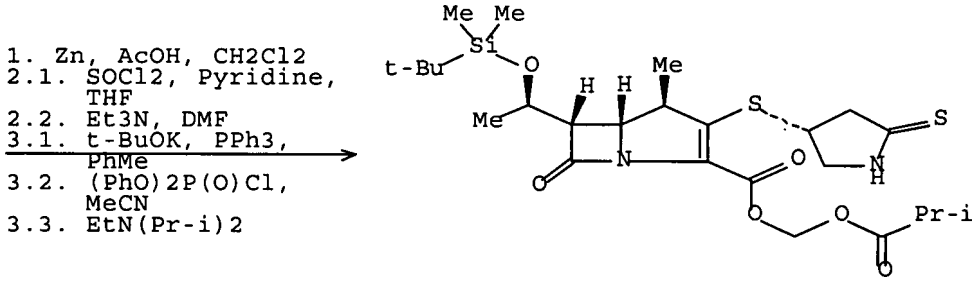


NOTE: 1) 0.degree., 2) -50 to -40.degree., then -20 to 0.degree., 3) -40 to -20.degree., then to 0.degree.

RX(46) OF 52 - 3 STEPS

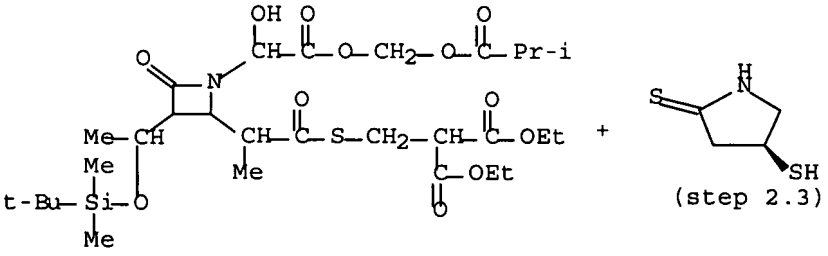


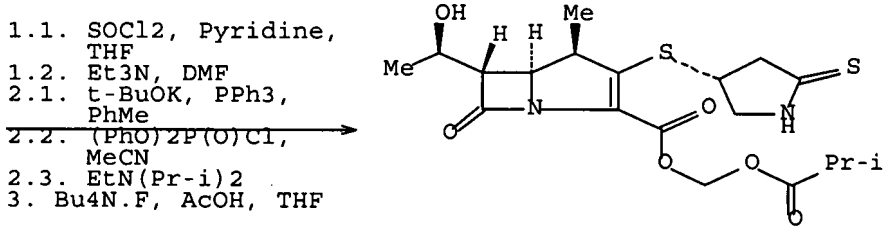
RX(46) OF 52 - 3 STEPS



NOTE: 1) 0.degree., 2) -50 to -40.degree., then -20 to 0.degree., 3) -40.degree., then -40.degree., then -20 to -5.degree.

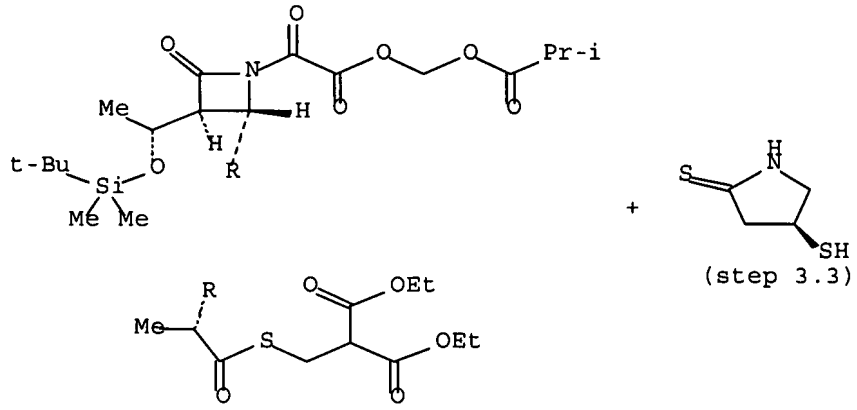
RX(47) OF 52 - 3 STEPS





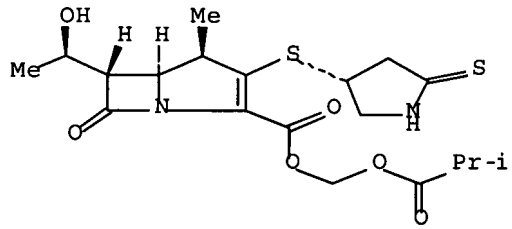
NOTE: 1) -50 to -40.degree., then -20 to 0.degree., 2) -40.degree., then -40.degree., then -20 to -5.degree., 3) room temp.

RX(48) OF 52 - 4 STEPS



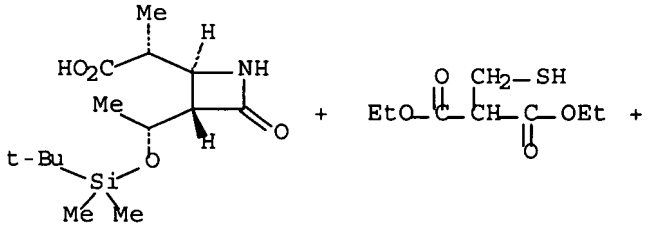
RX(48) OF 52 - 4 STEPS

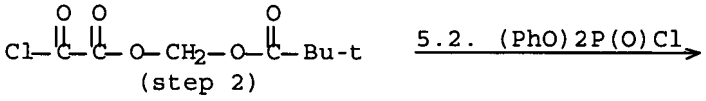
1. Zn, AcOH, CH2Cl2
2.1. SOCl2, Pyridine, THF
2.2. Et3N, DMF
3.1. t-BuOK, PPh3, PhMe
3.2. (PhO)2P(O)Cl, MeCN
3.3. EtN(Pr-i)2
4. Bu4N.F, AcOH, THF



NOTE: 1) 0.degree., 2) -50 to -40.degree., then -20 to 0.degree., 3) -40.degree., then -40.degree., then -20 to -5.degree., 4) room temp.

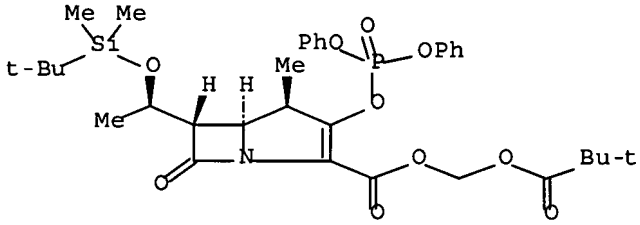
RX(50) OF 52 - 5 STEPS





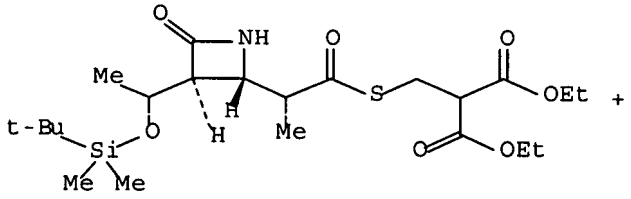
(step 2)

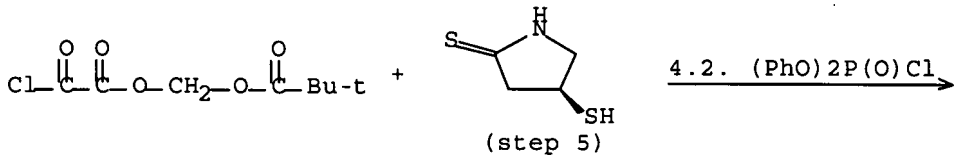
RX(50) OF 52 - 5 STEPS



NOTE: 1) room temp., 2) 0.degree., 3) 0.degree., 4) -50 to -40.degree., then -20 to 0.degree., 5) -40 to -20.degree., then to 0.degree.

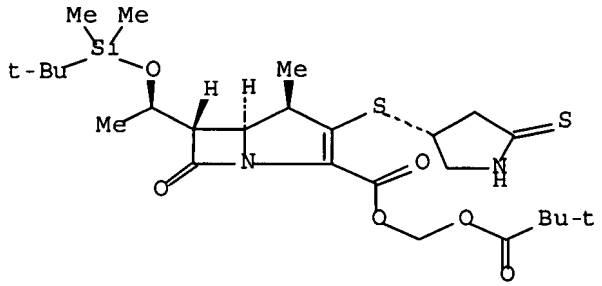
RX(51) OF 52 - 5 STEPS





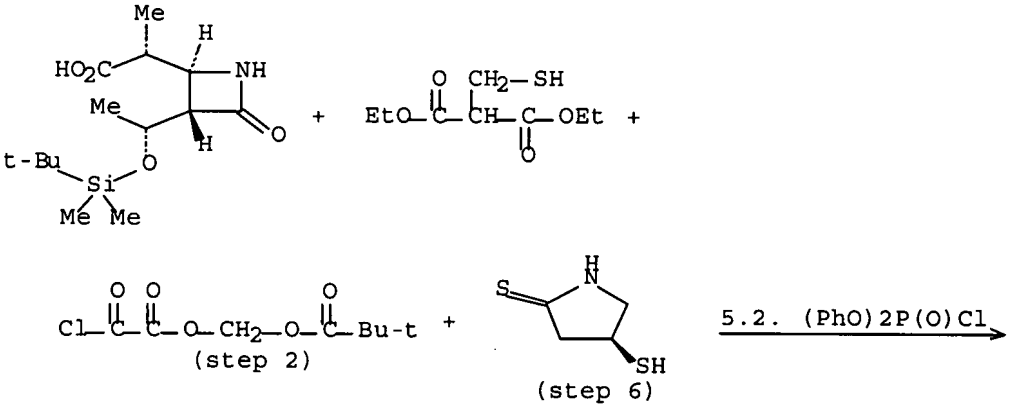
(step 5)

RX(51) OF 52 - 5 STEPS

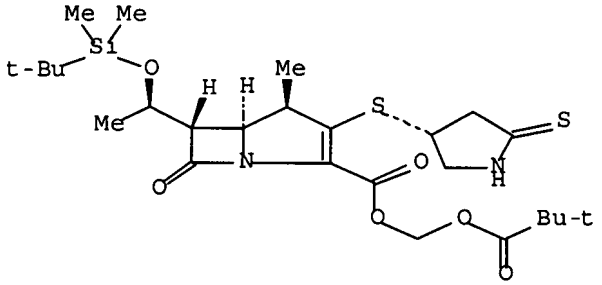


NOTE: 1) 0.degree., 2) 0.degree., 3) -50 to -40.degree., then -20 to 0.degree., 4) -40 to -20.degree., then to 0.degree., 5) -20 to 0.degree.

RX(52) OF 52 - 6 STEPS



RX(52) OF 52 - 6 STEPS



NOTE: 1) room temp., 2) 0.degree., 3) 0.degree., 4) -50 to -40.degree., then -20 to 0.degree., 5) -40 to -20.degree., then to 0.degree., 6) -20 to 0.degree.

=> d his nofil

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     (FILE 'HOME' ENTERED AT 09:13:07 ON 15 JUN 2007)

     FILE 'REGISTRY' ENTERED AT 09:13:21 ON 15 JUN 2007

     FILE 'BEILSTEIN' ENTERED AT 09:13:25 ON 15 JUN 2007
L1             STR

     FILE 'CASREACT' ENTERED AT 09:16:18 ON 15 JUN 2007
L2           0 SEA SSS SAM L1 (     0 REACTIONS)
L3           0 SEA SSS FUL L1 (     0 REACTIONS)
               D QUE
               D COST

     FILE 'CAPLUS' ENTERED AT 09:18:20 ON 15 JUN 2007
               E US2005-533183/APPS
L4           1 SEA ABB=ON  PLU=ON  US2005-533183/AP
               SEL RN

     FILE 'REGISTRY' ENTERED AT 09:18:50 ON 15 JUN 2007
L5          18 SEA ABB=ON  PLU=ON  (100-39-0/BI OR 105318-28-3/BI OR 157429-42
               -0/BI OR 157542-49-9/BI OR 161715-24-8/BI OR 179337-57-6/BI OR
               18997-19-8/BI OR 2524-64-3/BI OR 682747-73-5/BI OR 692779-22-9/
               BI OR 692779-23-0/BI OR 692779-24-1/BI OR 692779-25-2/BI OR
               692779-26-3/BI OR 7087-68-5/BI OR 74-88-4/BI OR 75-77-4/BI OR
               994-30-9/BI)
               D SCA
L6             STR L1

     FILE 'CASREACT' ENTERED AT 09:24:41 ON 15 JUN 2007
L7           0 SEA SSS SAM L6 (     0 REACTIONS)
L8           4 SEA SSS FUL L6 (    90 REACTIONS)
               D SCA

     FILE 'CASREACT' ENTERED AT 09:25:21 ON 15 JUN 2007

     FILE 'CASREACT' ENTERED AT 09:25:29 ON 15 JUN 2007
               D QUE L4

     FILE 'CASREACT' ENTERED AT 09:25:39 ON 15 JUN 2007
               D QUE L8

     FILE 'CASREACT' ENTERED AT 09:25:59 ON 15 JUN 2007
               D QUE L3
               D QUE L8
               D L8 IBIB ABS CRD TOT
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